CORRELATION OF INDUCED SPUTUM EOSINOPHIL AND ABSOLUTE EOSINOPHIL COUNT IN ASSESSING THE CLINICAL SEVERITY OF BRONCHIAL ASTHMA

DISSERTATION SUBMITTED TO THE TAMILNADU

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DEPARTMENT OF THORACIC MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

MAY-2019

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I hereby certify that this dissertation entitled **"CORRELATION OF INDUCED SPUTUM EOSINOPHIL AND ABSOLUTE EOSINOPHIL COUNT IN ASSESSING THE CLINICAL SEVERITY OF BRONCHIAL ASTHMA"** is a record of work done by **Dr. LOKNATH B** , in the Department of TUBERCULOSIS AND RESPIRATORY MEDICINE , Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2016- 2018. This work has not formed the basis for previous award of any degree.

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DECLARATION BY THE CANDIDATE

I solemnly declare that this dissertation titled **" CORRELATION OF INDUCED SPUTUM EOSINOPHIL AND ABSOLUTE EOSINOPHIL COUNT IN ASSESSING THE CLINICAL SEVERITY OF BRONCHIAL ASTHMA "** submitted by me for the degree of M.D., is the record work carried out by me during the period of 2016-2018 under the guidance of **Prof. Dr.K.KRISHNAMOORTHY, M.D**, Professor and Head of the Department, Department of Thoracic Medicine, Tirunelveli Medical College, Tirunelveli. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, towards the partial fulfilment of requirements for the award of M.D.(Branch XVII) Tuberculosis and Respiratory Medicine examination to be held in May 2019.

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CERTIFICATE – II

This is to certify that this dissertation work title **"CORRELATION OF INDUCED SPUTUM EOSINOPHIL AND ABSOLUTE EOSINOPHIL COUNT IN ASSESSING THE CLINICAL SEVERITY OF BRONCHIAL ASTHMA"** of the candidate **Dr. B. LOKNATH** with registration Number **201627202** for the award of **M.D.,** Degree in the branch of **THORACIC MEDICINE (XVII).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows 19% p**ercentage** of plagiarism in the dissertation.

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PROTOCOL TITLE: CORRELATION OF INDUCED SPUTUM EOSINOPHIL AND ABSOLUTE EOSINOPHIL COUNT IN ASSESSING THE CLINICAL SEVERITY OF BRONCHIAL ASTHMA
PRINCIPAL INVESTIGATOR: DR.LOKNATH,B, MBBS
DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI.

Dear, DR.LOKNATH,B, MBBS Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 16.06.2017

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b) The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c) If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
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   e) Approval for amendment changes must be obtained prior to implementation of changes.
   f) The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g) Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

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CONTENT

ABBREVIATION

GINA	Global initiative for asthma
INSEARCH	Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis
WRA	Work-related asthma
EIB	Exercise-induced bronchoconstriction
FEV1	Forced expiratory volume in 1 sec
FVC	Forced vital capacity
PEF	Peak expiratory flow
PFT	Pulmonary function test
BHR	Bronchial hyper responsiveness
GERD	Gastro-oesophageal reflux
RSV	Respiratory syncytial virus
ETS	Environmental tobacco smoke
NHLBI	National heart, lung, and blood institute
SABA	Short acting beta agonists
LABA	Long acting beta agonists
OCS	Oral corticosteroids
ICS	Inhaled corticosteroids
AEC	Absolute eosinophil count

1. INTRODUCTION

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary in intensity over time and variable expiratory airflow limitation [1]. Asthma is not an uncommon disease, affecting 1–18% of the population in different countries [1]. In the last two decades, its prevalence has increased worldwide [2]. Asthma is a chronic inflammatory disorder of the airways due to involvement of many cells and cellular elements, resulting in hyper responsiveness of the airway which explains most of the symptoms of asthma [3].

Criteria for the diagnosis of asthma include history of variable respiratory symptoms and variable expiratory airflow limitations in spirometry. The asthma control and severity are usually assessed by subjective measures such as clinical assessment and quality of life questionnaires and objective measure including spirometry, peak expiratory flow rate and bronchoprovocation testing. [4] But according to current GINA guidelines severity of asthma is assessed by the level of treatment required to control symptoms and exacerbations.

Over the last decade, various non-invasive markers for measurement of airways inflammation have been used in monitoring asthma severity, such as exhaled nitric oxide, sputum differential cytology and serum eosinophilic cationic protein [5]. But regarding the use of biological markers for assessing the severity of asthma, only limited studies are available and the relation is not well established.

Eosinophils as proinflammatory agents are thought to have an important role in the pathogenesis of asthma. In asthmatics, eosinophils and their mediators are consistently identified [6] . Sputum and blood eosinophilia are the biomarkers indicating an eosinophilic airway inflammation .

Not much data is available regarding the relation of clinical symptoms and functional parameters to these biomarkers of airway inflammation. Therefore, this study was done with the intention to find the correlation between sputum and absolute eosinophil count with severity of asthma.

2. AIM AND OBJECTIVES

AIM

To study the correlation of sputum eosinophil count and absolute eosinophil count in assessing the clinical severity of Asthma.

OBJECTIVES

1. To assess the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation.
2. To assess the correlation between the sputum eosinophil and absolute eosinophil count.

3. REVIEW OF LITERATURE

Asthma is a chronic inflammatory disorder of the airways causing bronchial hyper-responsiveness that is characterized by variable and recurring symptoms and airflow obstruction. For past several decades, asthma prevalence is increasing throughout the world. The major focus of asthma investigations and treatment were on allergic mechanisms for many years. Recent studies in epidemiology, natural history and pathogenesis have clearly demonstrated that asthma is a heterogeneous disease, with complex pathobiologic mechanisms with multiple aetiologies and contributing cofactors.

EPIDEMIOLOGY

Asthma is common affecting 1–18% of the population in different countries. Its prevalence has been steadily increasing over time [1].
Estimates of 'current asthma symptoms' among adults give variable values worldwide, ranging from less than 1% in Tunisia to more than 25% in Australia and Wales.[7]

In the Global Initiative for Asthma (GINA) estimates, prevalence of asthma was estimated to be 3.5% of the total population in Southern Asia (Bangladesh, Bhutan, India, Nepal, Seychelles and Sri Lanka).[7]

The burden of asthma in India is such that about one tenth of the individuals currently suffering from asthma worldwide are Indians.[1,9] The prevalence of asthma in India is estimated to be 3-38% in children and 2-12% in adults,[10] making it the most common chronic disorder among children.

According to the recent Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis (INSEARCH), the prevalence of asthma in India is estimated to be 2.05% among those aged >15 years and the national burden of asthmatics is estimated to be 18million[8].

MORTALITY AND MORBIDITY OF ASTHMA

Asthma causes limitations in daily activities, loss of school and work days, lung function impairment, reduced quality of life, and an adverse socioeconomic burden.

About 15 million disability-adjusted life years are lost annually due to asthma, which represents 1% of the total global disease burden[1].

Annually about 489,000 deaths are attributable to asthma[11] and the majority of it occur in low- and middle-income countries, particularly Oceania, South and Southeast Asia, the Middle East, and Africa [12].

Patients from these countries have more severe symptoms than others, possibly due to incorrect diagnosis, poor access to health care, poor adherence to therapy, exposure to environmental irritants and genetic susceptibility.[13]

ASTHMA SUBTYPES

Asthma is triggered and aggravated by many different sources. Subtypes can be described demographically by age of onset, type and place of exposure and in terms of the pathophysiology of the underlying inflammation.

Asthma has been classified

1. According to Age (Childhood-onset and Adult onset asthma).

Childhood-onset asthma: beginning during childhood, it has a peak prevalence of 10%is among children of age 5–9 years [14]. The "allergic triad" of asthma, atopic dermatitis and allergic rhinitis has been described in them. There seems to be some progression of atopic dermatitis and food allergy during infancy to asthma and/or allergic rhinitis during childhood [15]. Complete resolution of symptoms by adulthood is expected in approximately 58% of the children with asthma and continuous infrequent episodic asthma in 11% [16]. Male gender was a significant predictor of asthma remission [17].

Adult-onset asthma : It is the onset of symptoms in an adult with no pre-existing respiratory symptoms, but the age of onset has not been clarified [17] . Risk factor for late onset asthma includes ageing, women, obesity, occupation and mood disorder.

2. Based on the location of the exposure.

- Occupational asthma (new-onset asthma attributed to the workplace environment)
- Work-related asthma (WRA) (pre-existing or concurrent asthma worsened by factors related to the workplace environment)[18–20].

3.Based on the route of inflammatory response.

Allergic asthma is mediated by immunoglobulin E (IgE) reactions to airborne allergens. Common IgE-mediated allergens are dust mites, pet dander, cockroaches, moulds and grass pollens [21]. Symptoms are usually not severe and begin before 20 years of age and do not progress; however, acute severe or even fatal reactions can occur in heavy exposure [22].

Intrinsic or Non-Allergic Asthma does not involve an identified IgE response [23]. Common in middle-aged and older adults, intrinsic asthma is

more persistent and is more likely to progress in severity and become irreversible, than allergic asthma [22].

Irritant asthma is caused by non-corrosive chemicals that directly causes inflammation of both the upper and lower respiratory tract [24]. Irritants include a wide variety of chemicals that are found in the home, workplace, and outdoor environment. Common indoor irritants include solvents found in paints and glues, chlorine, bleach, and ammonia in household cleaners, hydrochloric and sulphuric acid, floor sealants, formaldehyde, capsaicin found in hot peppers and metal-working fluids [24]. Common outdoor air pollutants are by-products of fuel combustion including ozone, fine particulate matter, nitrogen dioxide, and sulphur dioxide [25]. Asthma can also be exacerbated by other extrinsic physical factors.

Exercise-Induced Bronchoconstriction (EIB) is defined as the transient narrowing of the lower airways after vigorous exercise in persons with or without the diagnosis of chronic asthma. The diagnosis of EIB usually requires a 10%–15% decrease in forced expiratory volume in 1 s (FEV1) (pulmonary function test) after exercise [20].

RISK FACTORS

Risk factors for the development of asthma are broadly divided into two factors

A. Host factors

1. Age and sex
2. Socioeconomic status
3. Racial and ethnic factors
4. Genetic polymorphisms
5. Other atopic conditions
6. Obesity

B. Environmental factors

1. Aeroallergens
2. Infections
3. Occupational exposures
4. Environmental pollutants
5. Outdoor pollution
6. Indoor pollution

Environmental tobacco smoke/In utero exposure to smoke

Solid fuel combustion

7. Diet: Processed foods

Breastfeeding (Protective role)

HOST FACTORS

Age and Sex*:* On an average, asthma occurs with equal frequency in both sexes. There is a male predominance in children, being twice common in boys than in girls before 14 years of age [26]. As the age advances, the sex difference disappears. In adults a higher incidence in women is seen because of hormonal factors. Asthma is more common in children of 5 to 14age group. Because of its chronic nature, the cumulative prevalence of asthma increases as the age advances. Earlier it was believed that asthma in children will be cured after when grow up. But the disease cannot be labelled as "eliminated" although about a third to half of the children may become asymptomatic as they grow. Later in life a large number of these children develop symptoms. New onset of asthma can also arise in elderly. Non-atopic and fixed airways were common with higher mortality.

Genetic Factors*:* Asthma has a strong genetic predisposition. The role of genetic factors is indicated with the presence of a history of asthma and other allergies in the first degree relatives of patients. In a study on cumulative incidence of asthma in twins identical twins were found to have a very high relative risk (17.9) of asthma [27].The evidence was strongly considered in favour of the genetic predisposition. Genetic factors are important determinants of susceptibility to allergic diseases and asthma. In asthmatic patients, no single gene defect is identifiable. Multiple genetic polymorphisms associated with clinical asthma and/or Bronchial hyper

responsiveness (BHR) have been identified, some of which may actually affect the bronchodilator responsiveness [28-31]. Many genes are found to modify the treatment response to antiasthma drugs [32-35]. Their role in determining the in utero development and early life susceptibility to allergies have been highlighted in recent studies [36]. This has resulted in better endophenotying, prognosticating and predicting of treatment responses [36]. It can be therefore, anticipated that the gene polymorphism may play an important role in future in planning and improving the management of asthma [34-37].

More than 100 genes have been studied as biologic candidate genes based on plausible biologic mechanisms in asthma or locations in chromosomal regions linked to asthma. The most replicated candidate genes appear to be related to broad categories of lung development (e.g., ADAM33), the type 2 T helper cell (Th2) inflammatory pathway (IL4, IL13, IL4R), innate immunity(HLA-DRB1, HLA-DQB1, CD14), and cellular inflammation(TNF, FCER1B, DPP10) . In addition, candidate genes as potential pharmacogenetic loci that modify responses to pharmacologic therapy have also been evaluated. This include genes within the glucocorticoid receptor complex pathway, the leukotriene pathway (LTC4S), the β2-adrenergic receptor gene (ADRB2), and the Th2 inflammatory pathway signalling (IL4R).

Other Host Factors*:* There is difference in prevalence of asthma in different racial and ethnic populations. Some of these differences could be attributed to different genetic polymorphisms. Different environmental exposures may also influence the prevalence differences. Presence of nasal (allergic rhinitis) and skin (atopic dermatitis) atrophies, sinusitis and nasal polyposis is frequently associated with asthma possibly because of a common pathogenesis. Nasal allergy in particular is said to exist with asthma as an essential companion—"one airway–one disease". Presence of obesity is also a recognized risk factor [31] for asthma, supposedly mediated through the release of leptins.

GERD

Epidemiological evidence for the association suggest that about three-fourth of the asthmatics, have acid gastro-oesophageal reflux, increased frequency of reflux episodes, or heart burn, and about 40 per cent have reflux oesophagitis. A recent report says that 24-hours PH monitoring oesophageal tests have abnormal results, in around 67% of asthmatics without having reflux symptoms. Prevalence of gastro-oesophageal reflux in asthmatics can be summarised as follows [72 -83].

- 57% of asthmatics have heartburn
- 41% of asthmatics note reflux-associated respiratory symptoms
- 82% of asthmatics have abnormal oesophageal acid contact times

• 43% of asthmatics have oesophagitis.

• Heartburn is more prevalent in asthmatics over 65 years of age (35%) compared with non-asthmatics 18-34 years of age (23%).

• Heartburn is associated with a higher rate of future asthma hospitalisation.

• Subjects reporting nocturnal GER have higher asthma prevalence rates and symptoms of obstructive sleep apnoea.

• Proximal oesophageal acid exposure is present in 48% of asthmatics.

• In children: abnormal oesophageal pH tests are present in 62% and GER is a risk factor for asthma.

PSYCHOLOGICAL FACTORS

The relationship of asthma and psychological factors has been in a great deal of controversy. Many patients with asthma acknowledge the exacerbations to be provoked by psychological events, such as shock, bereavement, or excitement. However, such factors are rarely the dominant cause of disease.

ENDOCRINAL FACTORS

A number of patients complain exacerbation of symptoms during or preceding menstruation, although the exact role of hormones in asthma has

not been defined. It is suggested that oestrogen plays a role in the pathophysiology of asthma as long-term use and/or high doses of postmenopausal hormone therapy have been associated with increased risk of asthma [84]. Influence of thyroid hormones on asthma has also been observed. Hyperthyroidism is accompanied by manifestations suggesting over stimulation of the sympathetic system and this is a contraindication for use of β-2 agonists. Bronchodilator response is impaired in the presence of excess thyroid hormones, which improves after euthyroid state is achieved.[85]

ENVIRONMENTAL FACTORS

Several environmental exposures have been implicated in the development of asthma, such as aeroallergens, occupational agents, tobacco smoke, outdoor and indoor air pollutants and possibly infectious agents. Some of these agents may also act as "precipitating" or "aggravating " factors for asthma.

Allergens: Family history of atopy is the strongest risk factor for asthma. This increases the risk of developing allergic rhinitis by fivefold and the risk of asthma by threefold to fourfold. Many air borne pollens, fungal spores, home dust mite, insect debris, cat and dog dander have been implicated as independent risk factors for asthma [86-89]. Early exposure to

cat and dog dander has been reported as protective against allergen sensitization in some studies, while others suggest that it increases the risk.[89-91].

Infections: Infections like respiratory Syncytial Virus (RSV) and parainfleunza virus infections are known to cause asthma in children [92].On the other hand, early childhood infections are reported to protect from asthma (Hygiene hypothesis),[94] possibly explaining the lower asthma prevalence in the developing countries, including India, due to higher occurrence of childhood infections. The "hygiene hypothesis" is based on the concept that exposure to airway infections and allergens early in life causes maturation of T-helper 1(Th1) lymphocytes over Th-2 lymphocytes, thereby decreasing the risk of allergies.[93] . The theory has been further supported by some studies [41,42].The issue is unresolved. Genetic susceptibility of an individual may also contribute to this. The common organisms, which have been cultured from bronchoalveolar lavage are the viruses(adenovirus, parainfluenza, RSV and influenza), Mycoplasma and Chlamydia indicating that they may have an important role in asthma development, airway inflammation and remodelling.[43] Of various parasites, only hook worm infestations have been shown to reduce the risk.[44]

Occupational Exposures:

Occupational asthma is the commonest industrial lung disease in the developed world.10% of adult onset asthma may account for it. Exposure to chemical vapours, irritant gases, metal fumes and other exhausts amongst persons engaged in different occupations may cause airway sensitization and increased production of IgE, which commonly manifest as occupational asthma[47-49]. Occupational sensitization is also responsible for the precipitation of asthma. Occupational asthma occurs generally after an exposure period of month to years in sensitive individuals [50,51] . Both IgE mediated and cell-mediated immunological reactions are involved [52].

Environmental Pollution and Smoking:

Exposure to environmental air pollutants in both outdoor and indoor conditions is an important cause of increased asthma exacerbations.[51] Domestic combustion of solid fuel for cooking is an important cause of indoor air pollution in India as well as in several third-world countries. In children, combustion exhausts are responsible for increased respiratory infections as well as lung function impairment. However, their role in the development of asthma remains debatable[54] .Environmental Tobacco Smoke (ETS), is another important cause of increased asthma morbidity amongst both children and adults [55-57]. In utero exposure of the fetus to smoke from a smoking mother is reported to influence the lung

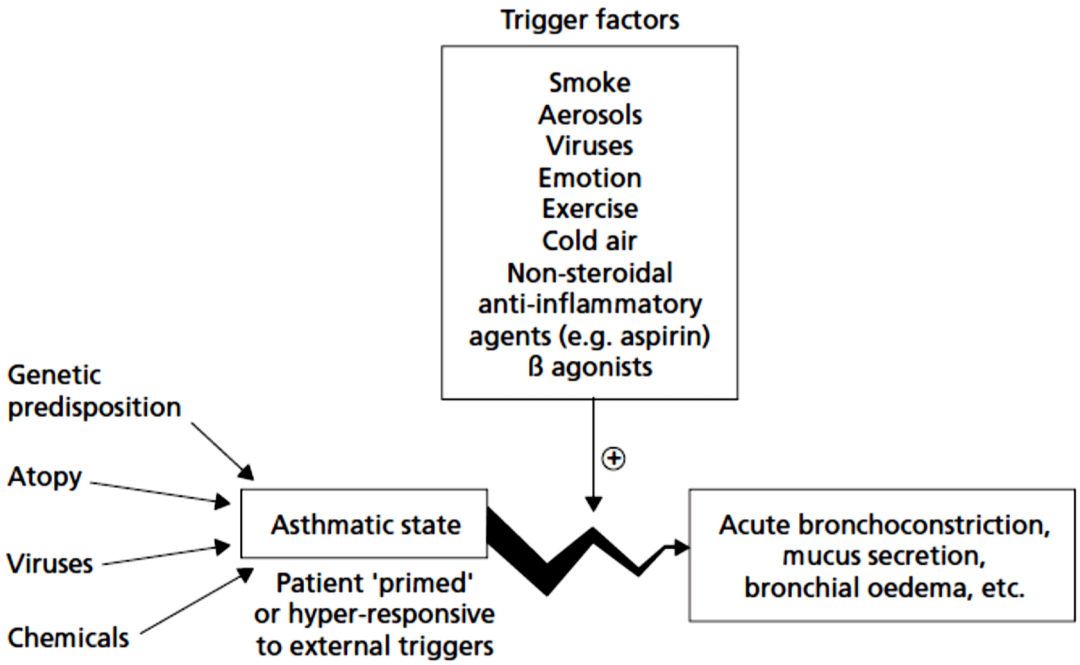
development and to be responsible for persistent wheezing problems in children in the first year of life [58]. There is no good evidence to attribute the development of asthma to ETS exposure.

Diet :

Food sensitivity is an important factor in the development of allergies .In the first 1 or 2 years of life. Breastfeeding has been advocated as a method of preventing allergy and asthma. With breastfeeding there is a decreased risk (about 20%) for asthma [59] .Impact of exclusive breastfeeding in children till 6 months of age has shown that the introduction of milk other than breast milk before the age of 4 months of age is a significant risk factor for increased likelihood of bronchial asthma [60] . However, another study has shown an increased risk of wheezing, in child with atopy, particularly in asthmatic mothers [60].

There are some reports that says regular consumption of oily fish is associated with a reduced risk of asthma in children. But subsequent studies have not shown clinical benefits of supplemental ω3 fatty acids over a 6 months period [61,62] . Further, it has been hypothesised that higher concentrations of vitamin intake are associated with a decreased incidence of asthma as serum levels of IgE are decreased in them[64] .Recent experimental study showed a reduced risk with intake of lectins (wheat germ agglutinin from whole wheat products).[65]

Asthma involves a complex interplay of different mechanisms, which results in a common clinical presentation of widespread airway obstruction. There are huge epidemiological and clinical variations in the disease spectrum of asthma which are now unfolding. [66,67]



SCHEMATIC DIAGRAM SHOWING PREDISPOSING FACTOR THAT CAUSE/ STIMULATE THE HYPERRESPONSIVE AIRWAY

PATHOPHYSIOLOGY OF BRONCHIAL ASTHMA

Recent advances in the understanding of pathophysiology indicate that it is a heterogeneous disorder with multiple triggers with the mechanism virtually common to all asthmatics which include airways inflammation and hyperactivity to a broad range of stimuli.

The chronic allergic response is a continuous process of IgE generation, mast cell activation and eosinophil recruitment. These processes are organised by T lymphocytes. In atopic individuals, T lymphocytes receive an allergen-specific signal from highly specialised antigen presenting cells, called dendritic cells. Present at mucosal surfaces, dendritic cell inhale allergens like cigarette smoke, house dust mites, pollen, viral infection, fungi, etc. and migrate to the regional lymph nodes and present allergens, together with major histocompatibility antigen II, to lymphocytes. Presentation of allergen peptides to the T cell usually along with the essential engagement of co-stimulatory molecules (B7 and CD28) results in the differentiation of the naive T cell to one that generates a range of cytokines which up regulate cells and antibodies involved in the allergic response. CD4+ lymphocytes of the Th2-typeare activated and clonally expand. A number of cytokines is then released. The genes for these cytokines are encoded in a small region on the long arm of chromosome 5 and a number of them (IL-4, IL-5, and GMCSF)are co-ordinately regulated.

While Th2 lymphocytes produce these cytokines, Th1lymphocytes are involved in cell-mediated immunity. A number of Th2-derived cytokines are involved in mast cell, basophil, and eosinophil recruitment and maturation. IL-4 andIL-3 play a particularly important role in this arm of the immune process by interacting with B lymphocytes and changing the immunoglobulin isotope to be secreted from the short term protective antibody IgM to the allergic antibody IgE. As with dendritic T cell interactions, effective signalling to B cells requires an interaction with the Th2 cell and involves antigen presentation and engagement of a second set of co-stimulatory molecules (CD40 and its ligand, CD40L). If T and B cell interact in the presence of antigen, IL-4 or IL-13, and co-stimulatory molecules, allergen-specific IgE is generated. If IL-4 or IL-3 is present, but cell-cell contact does not occur, only non-specific IgE is generated. Thus IgE has the important role of linking allergen recognition to cell signalling in a variety of cells. IL-4 produced by Th2 lymphocytes 'fuels' the inflammatory reactions in the airways and leads to production of further Th2 lymphocytes.

A strong genetic component plays important role in the form of an ability of a susceptible individual to recognise an environmental allergen as foreign and mounts an allergic immune response through the human lymphocyte antigen(HLA or MHC class II) molecules. The component of the gene involves the genes responsible for cytokine response.

Allergen specific IgE binds to IgE receptors on several inflammatory cell types such as eosinophils, mast cells, and macrophages. High affinity IgE receptors are an important link between the presence of specific antigen in the microenvironment and activation of mast cells and other cells. When antigen binds an adequate number of these receptors to initiate receptor clustering, signal transduction occurs. The IgE receptor is composed of four chains: an alpha chain, a beta chain, and two gamma chains. While alpha chain binds IgE, gamma chains initiate intracellular signal transduction; however, the specific mechanism of transduction is not established. The inflammatory cells then release various inflammatory mediators including 5-lipooxygenase products and protease, which accentuates airways' inflammations. Leukotrienes along with other products cause bronchoconstriction and other changes characteristic of bronchial asthma. Mast cell proteases are also important players in the inflammatory process. Neutral endopeptidase (NEP) is a major enzyme of importance in limiting the biologic activity of small peptide mediators such as substance P or neurokinin A. In modifying the biology of an asthmatic response beta-adrenergic receptor and nitric oxide represent two important effector mechanisms. It is now understood that role of nonmuscular airway obstruction is not less important although smooth muscle constriction can lead to airways obstruction. Thickening of the airway wall due to infiltration with inflammatory cells and alteration in the amount,

engorgement of the bronchial blood vessels and type of collagen deposited in the airway leads to airway wall remodelling. It results in enhanced degree of obstruction for a given level of smooth muscle activation in the remodelled wall. Bronchial blood vessel engorgement could account for a significant component of asthmatic airway narrowing under certain circumstances. The presence of intraluminal fluids including mucous substances could make it more difficult for individuals to clear secretions from their airway further obstructing the airways. During the last decade, relationship between airway inflammation and the development of airway hyper responsiveness and clinical asthma has been well established. Exposure to oxidant pollutants, some chemicals, antigens, and viral respiratory tract infections are all associated with inflammatory stimuli associated with the development of airway hyper responsiveness.

EOSINOPHILS

Eosinophilia and elevated IgE levels are common findings in adults with asthma and also in infants who subsequently develop asthma. It is possible that neutrophil-induced inflammation is important in the early stages of wheezing in infants. The number of activated eosinophils is associated with epithelial shedding and thus rated to asthma severity. Their development is dependent on T cell function. The IL-5 specifically stimulates eosinophil differentiation. They have receptors for IgG, IgA,

and IgE on their cell surface. These cells are able to produce many mediators that are responsible for the disordered airway function characteristic of asthma. These substances include:

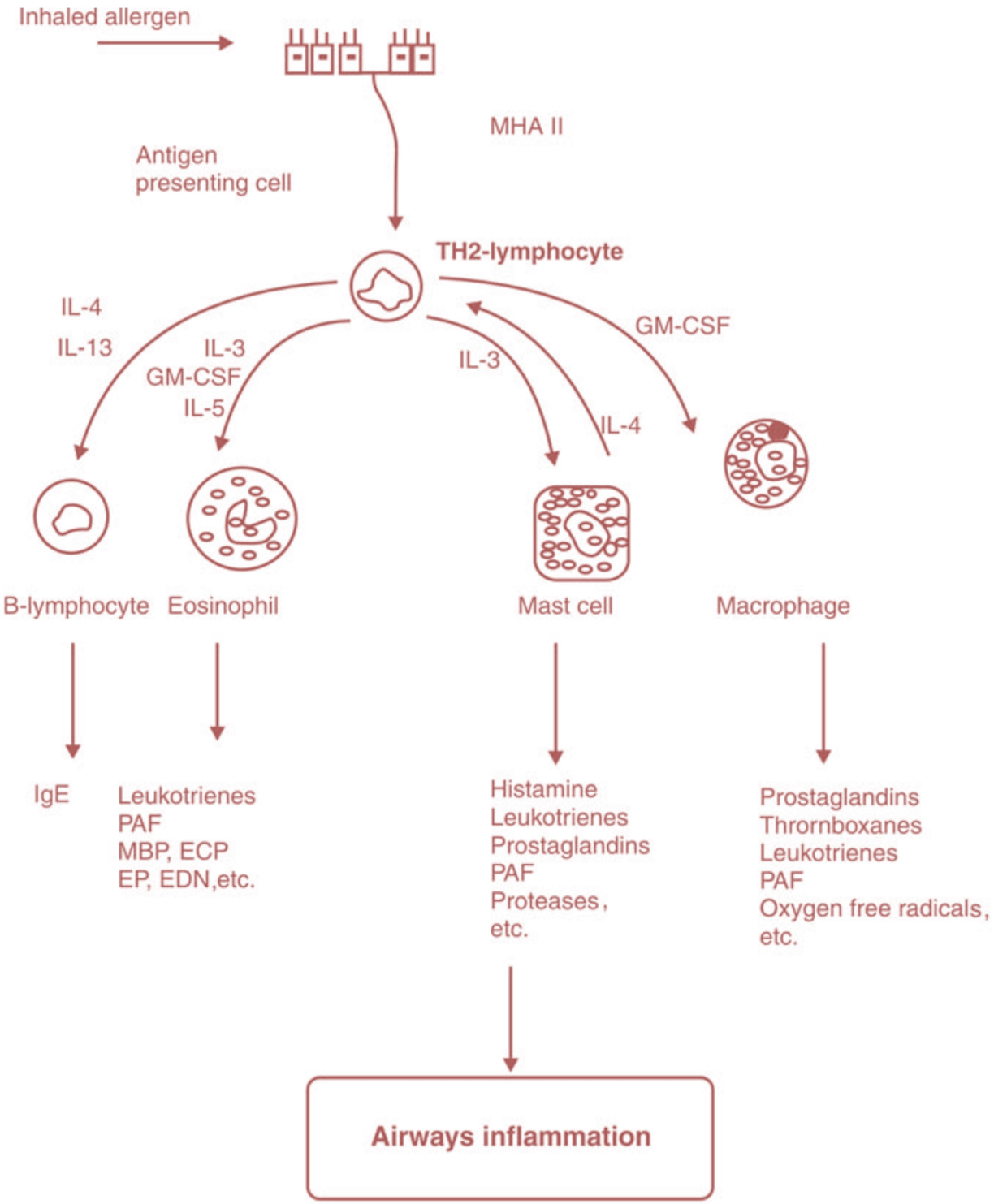
- Platelet activating factor
- LTB4
- LTC4
- PGE2
- 15-HETE
- Oxygen radicals and
- Four cytotoxic proteins i. Major basic protein (MBP) ii. Eosinophil cationic protein (ECP) iii. Eosinophil-derived neurotoxin (EDN) and iv. Eosinophil peroxidase (EPO).

All these mediators are released by activated eosinophils. The release of these mediators results in bronchoconstriction, epithelial damage and recruitment and priming of other inflammatory cells. IL-3, IL-4, IL-5 and GM-CSF (Granulocyte macrophage-colony stimulating factor) released from a number of cell types in the airways including activated T cells of the TH2 type, and mast cells control eosinophil maturation and priming. Charcot-Leydon crystal protein present in the eosinophis possesses lysophospholipase activity.

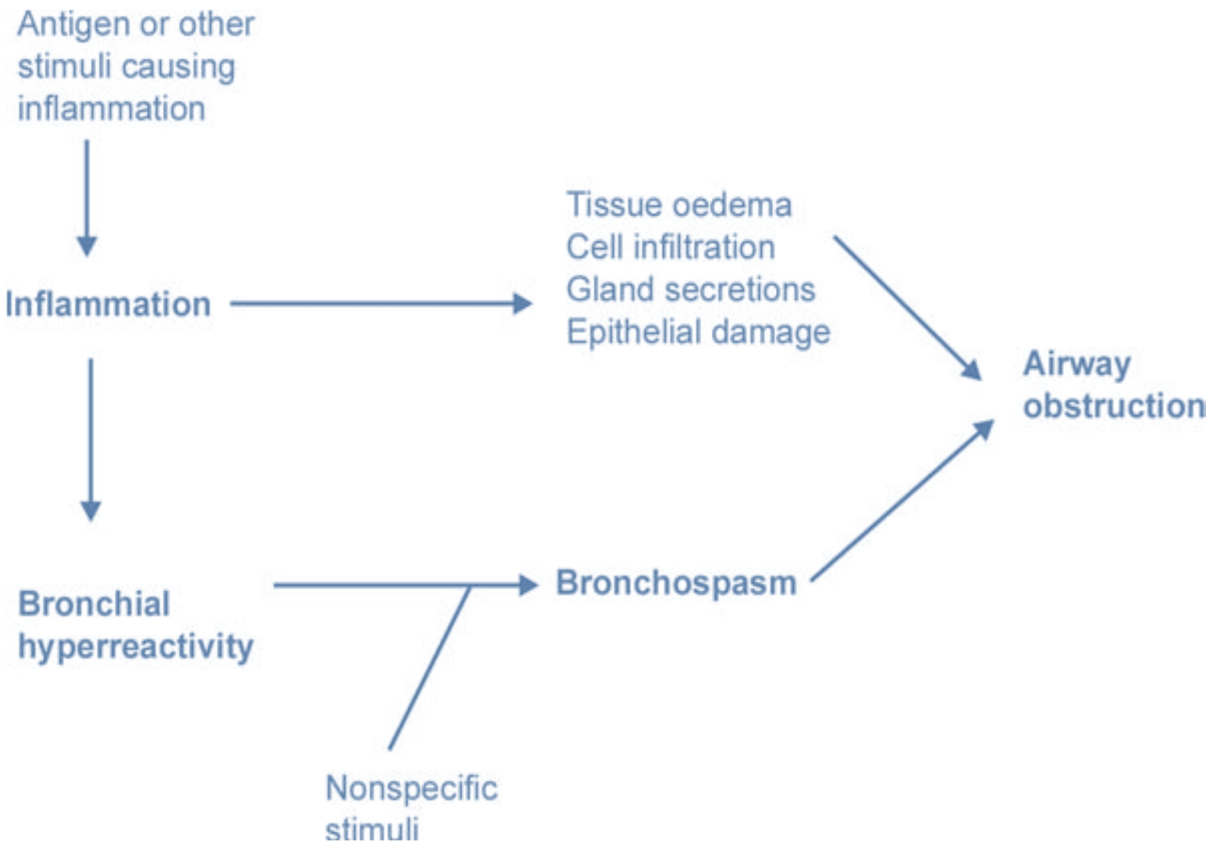
Eosinophils have characteristic granules and granular proteins. The granule has crystalloid core and matrix. The four cytotoxic proteins are present in the granules. The genes of these proteins are cloned. The cDNA for MBP showed the existence of a pro-MBP molecule that has an acid-rich portion and a basic MBP portion. EDN and ECP are both ribonucleases. In addition, ECP is a potent helminth toxin. EPO is a member of the peroxidase multigene family that includes myeloperoxidase, thyroid peroxidase, and lactoperoxidase. The MBP, deposited in the damaged areas of the epithelium, is toxic to it and is elevated in the sputum of patients with asthma. It has also been shown that not only MBP, but also other cytotoxic drugs in the presence of halide and hydrogen peroxidase, damage bronchial epithelium. Experimental studies have shown that eosinophil proteins, particularly MBP applied to respiratory epithelium stimulates smooth muscle contraction and increase the sensitivity of the smooth muscle to acetylcholine. This suggests that eosinophil is an effector of the changes of bronchial hyperreactivity *in vivo*.

While the pathogenesis of occupational asthma, intrinsic asthma and other forms of asthma is less clearly understood, these conditions are thought to involve a cytokine “cascade” similar to that involved in extrinsic or allergic asthma.

SCHEMATIC DIAGRAM SHOWING INFLAMMATORY RESPONSE TO ALLERGEN



MECHANISM OF AIRWAY OBSTRUCTION



DIAGNOSIS OF ASTHMA

Criteria for making the diagnosis of asthma according to GINA guidelines[1] includes:

1.History of variable respiratory symptoms

Generally more than one respiratory symptom occur, varying over time and in intensity. Symptoms are often worse at night and on waking and triggered by exercise, laughter, allergens, cold air.

2. Confirmed variable expiratory airflow limitation

I : Confirm presence of airflow limitation

- Confirm reduced FEV_1/FVC, at least once, when FEV_1 is low. (FEV_1/ FVC ratio is normally n>0.90 in children and>0.75 – 0.80 in healthy adults,)

II : Confirm lung function variation is greater than healthy individuals

Greater the probability that the diagnosis is asthma, when greater is the variation, or the more times variation is seen.

- Positive bronchodilator reversibility
  - Adults: increase in FEV1 of >12% and >200 mL from baseline, 10–15minutes after 200–400 mcg albuterol or equivalent (greater confidence if increase is >15% and >400 mL).
  - Children: increase in FEV1 of >12% predicted
- Excessive diurnal variability from 1-2 weeks
  - Daily diurnal PEF variability is calculated by recording twice daily PEF. It is ([the day's highest minus the day's lowest] / mean of the day's highest and lowest), and averaged over one week
  - Adults: average daily diurnal PEF variability >10%

- *Children*: average daily diurnal PEF variability >13%

- Significant increase in PEF or FEV1 after 4 weeks of controller treatment
  - Adults: increase in PEF by >20% or FEV1 by >12% and >200 mL from baseline after 4 weeks of treatment, without respiratory infections.
- Positive exercise challenge test
  - Adults: fall in FEV1 of >10% and >200 mL from baseline
  - Children: fall in FEV1 of >12% predicted, or PEF >15%
- Positive bronchial challenge test (usually only performed in adults) .
  - Fall in FEV1 from baseline of ≥20% with standard doses of methacholine or histamine, or ≥15% with standardized hyperventilation, hypertonic saline or mannitol challenge
- Excessive variation in lung function between visits (less reliable)

- Adults: variation in FEV1 of >12% and >200 mL between visits, outside of respiratory infections.
- Children: variation in FEV1 of >12% in FEV1 or >15% in PEF between visits (may include respiratory infections) .

ASSESSMENT OF ASTHMA

According to GINA guidelines, assessment of asthma include the assessment of asthma control (both symptom control and future risk of adverse outcomes), treatment issues (inhaler technique and adherence) and any co morbidities that could contribute to symptom burden and poor quality of life.

1. **Asthma control - two domains**
    - Assess symptom control over the last 4 weeks
    - Assess risk factors for poor outcomes, including low lung function
2. **Treatment issues**
    - Check inhaler technique and adherence
    - Ask about side-effects

- Does the patient have a written asthma action plan?
- What are the patient's attitudes and goals for their asthma?

3. **Co morbidities**

- Rhinosinusitis, GERD, obesity, obstructive sleep apnea, depression, anxiety

ASTHMA CONTROL

The level of asthma control is the extent to which the manifestations of asthma can be observed in the patient, or have been reduced or removed by treatment. [68,69]. The patient's genetic background, underlying disease processes, the treatment that they are taking, environment, and psychosocial factors, all determine it.[69]

The assessment of asthma control involves five essential steps: determining the current degree of control based on symptoms, recent exacerbations, reliever medication use, lung function and the risk of future adverse outcomes.

With this in mind, based on expert opinion, the NHLBI updated guidelines and the *Global Initiative for Asthma* (GINA) proposed a parallel scheme for asthma control. The NHLBI and GINA categorizations represent categorical interval variables with threshold values.

GINA guidelines accept some daytime symptoms (<2 times/week) in the definition of "controlled" asthma, whereas nocturnal symptoms defines a patient in the "partially controlled" category. The importance of control indices is underscored by the relationship between poor asthma control and substantial degrees of physical impairment and diminished quality of life, even after taking the baseline severity of asthma into account.[70]

Several different validated instruments exist for assessing asthma, including the Asthma Control Questionnaire, Asthma Control Test, Asthma Therapy Assessment Questionnaire, and Asthma Control Scoring System. All are useful because they direct history taking, provide goals for the management of symptoms, and guide adjustments in treatment.[71]

Symptom control			
In the past 4 weeks, has the patient had:	**Well-controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice a week?	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?			
• Reliever needed for symptoms* more than twice a week?			
• Any activity limitation due to asthma?			

RISK FACTORS FOR POOR ASTHMA CONTROL

Assess risk factors at diagnosis and periodically, especially for patients experiencing exacerbations. Measure FEV1 at start of treatment, after 3–6 months of controller treatment to record it as the patient's personal best lung function, then periodically for ongoing risk assessment. Having uncontrolled asthma symptoms is an important risk factor for exacerbations.

Additional potentially modifiable risk factors for flare-ups (exacerbations) include:

High SABA use (with increased mortality if >1 x 200-dose canister/month)

- Inadequate ICS: not prescribed ICS; poor adherence; incorrect inhaler technique
- Low FEV1, especially if <60% predicted
- Major psychological or socioeconomic problems
- Exposures: smoking, allergen exposure if sensitized
- Co morbidities: Obesity, rhinosinusitis or confirmed food allergy
- Sputum or blood eosinophilia
- Pregnancy

Other major independent risk factors for flare-ups (exacerbations)

- Ever intubated or in intensive care unit for asthma
- ≥1 severe exacerbation in last 12 months

Risk factors for developing fixed airflow limitation

- Lack of ICS treatment
- Exposures: tobacco smoke; noxious chemicals; occupational exposures.
- Low initial FEV1; chronic mucus hyper secretion; sputum or blood eosinophilia.

Risk factors for medication side-effects

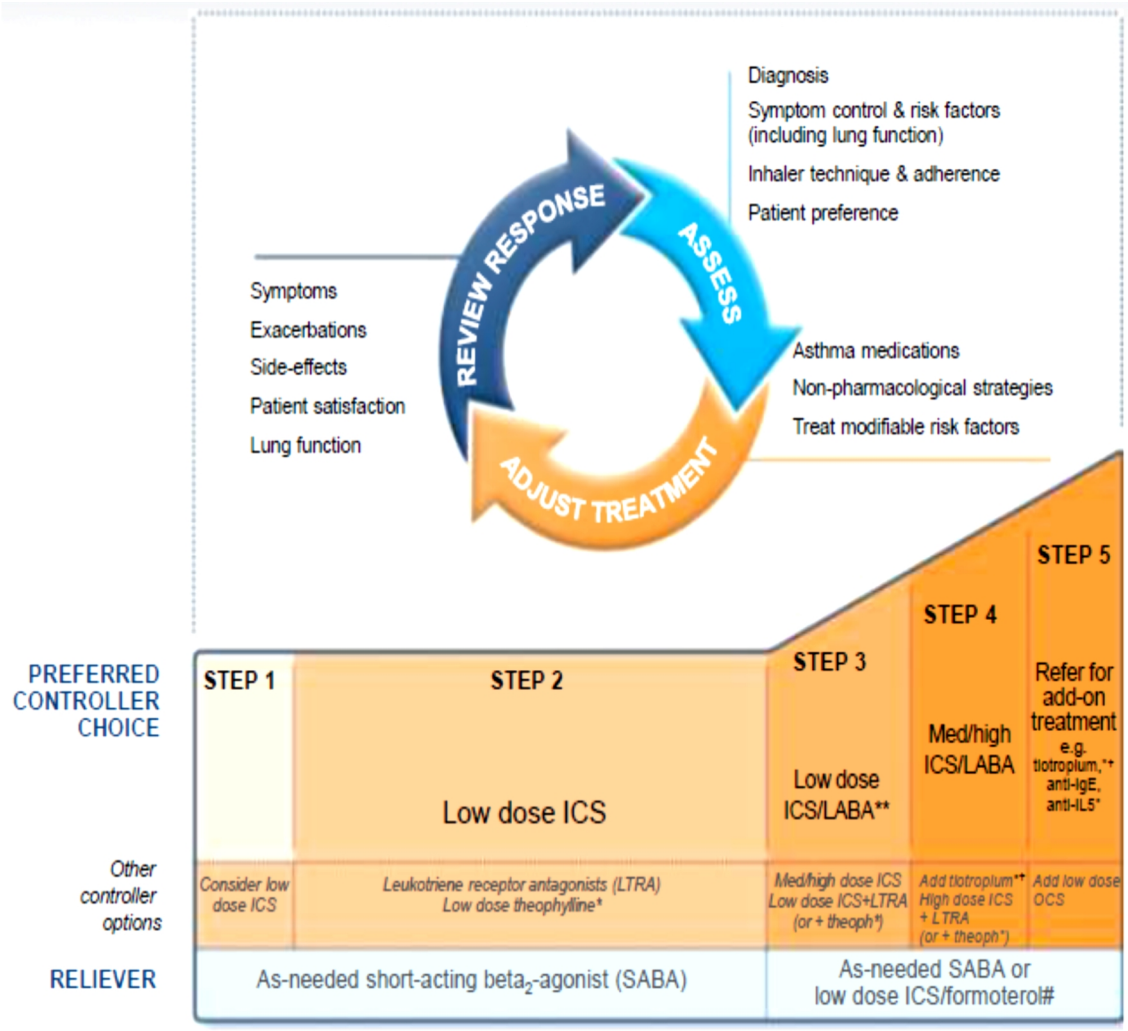
- *Systemic*: frequent OCS; long-term, high dose and/or potent ICS; also taking P450 inhibitors
- *Local*: high-dose or potent ICS; poor inhaler technique

According to GINA guidelines, Asthma severity can be assessed when the patient has been on regular controller treatment for several months. Mild asthma is asthma that is well controlled with Step 1 or Step 2 treatment i.e. with as-needed reliever medication alone, or with low-intensity controller treatment such as low dose ICS, leukotriene receptor antagonists .

Moderate asthma is asthma that is well controlled with Step 3 treatment e.g. low dose ICS/LABA.

Severe asthma is asthma that requires Step 4 or 5 treatment e.g. high-dose ICS/LABA, to prevent it from becoming ‘uncontrolled’, or asthma that remains ‘uncontrolled’ despite this treatment.

STEPWISE APPROACH TO CONTROL ASTHMA



Interest has been growing in the use of non-invasive methods for the assessment of airway inflammation in subjects with asthma based on expert opinion. To date sputum induction is the one of the non-invasive measure of airway inflammation that has a clearly proven role in asthma management. Induced sputum cell count and mediator measurements have been particularly well validated. A variety of mediators can be measured in the sputum supernatant of patients with asthma like eosinophil-derived proteins, cytokines and remodelling-associated proteins. Sputum eosinophilia (i.e., >3%) is a classic feature of asthma. A minority of patients present a non eosinophilic cellular pattern. The percentage of sputum eosinophils has proved to be useful in predicting short term response to inhaled corticosteroids. Sputum induction is a procedure that is generally well-tolerated and safe and a European Respiratory Society (ERS) Task Force has published a comprehensive review on sputum methodology. The widespread application of induced sputum in the investigation of asthma, mainly in moderate to severe asthma, has provided insight into the relationship between airway function and airway inflammation. This has lead to the proposal of new disease phenotypes and their response to current treatment, offering an additional tool to guide the clinical management of patients with asthma.

4. **MATERIALS AND METHODS**

The present study “Correlation of induced sputum eosinophil and absolute eosinophil count in assessing the clinical severity of bronchial asthma ” was conducted in Department of Thoracic Medicine, Tirunelveli Medical College Hospital after obtaining approval from Tirunelveli Medical College Institutional Ethical Committee (TIREC).

STUDY DESIGN :

Prospective study

STUDY POPULATION :

Patients were selected from outpatient and inpatient departments of Thoracic medicine, Tirunelveli Medical College Hospital.

STUDY DURATION :

The study was carried out between JUNE 2017 to JUNE 2018.

METHODOLOGY

Inclusion Criteria :

All stable asthmatic patients of 18–60 years of age.

Exclusion Criteria :

1. Acute exacerbation.
2. Clinical features and spirometry suggestive of chronic obstructive pulmonary disease.
3. Not willing to give consent.
4. Patients not able to perform spirometry correctly.
5. Patients with history of recent myocardial infarction.
6. Patients on chronic corticosteroid therapy.

After obtaining informed written consent, demography, history, radiological findings of the patients and relevant investigations were recorded.

- Demography of the patient includes age, sex, BMI, occupation.
- History of smoking, clinical symptoms and signs, co morbid conditions were obtained.

Assessment of severity of asthma

The severity of asthma was assessed according to the GINA criteria.[1] This includes

1. Asthma control questionnaire consists of frequency of diurnal and nocturnal symptoms, frequency of short acting beta 2‑agonist used, interference with daily activity in past 4 weeks
2. Number exacerbation per year and
3. Spirometry.

Spirometry

Patients were subjected to PFT with flow sensing winspiro PRO 5.7 spirometer. The obstruction severity was classified based on the FEV1‑based criteria recommended by the European Respiratory Society and the American Thoracic Society . Patients were assessed for post bronchodilator reversibility after administering 200 μg of inhaled salbutamol and by repeating the test after 15 min from the baseline. The degree of reversibility in forced expiratory volume 1 s (FEV1) of 12% and 200 ml from the prebronchodilator value was considered as diagnostic for asthma as per GINA guidelines.[1]

PROCEDURES AND COLLECTION OF SPECIMENS

According to the inclusion criteria patients were selected . Participants were categorized according to the GINA criteria based on clinical symptoms and pulmonary function test.

Blood samples was collected for absolute eosinophil count and induced sputum samples for eosinophil count.

INDUCED SPUTUM COLLECTION

STEPS

1. Procedure was explained in detail to the subject (rinse mouth before procedure, saline inhalation with tidal breathing, saliva handling during inhalation; after 5 min intervals cough and try to expectorate into the sputum cup).

2. Set nebuliser (output ~1 $mL \cdot min^{-1}$), fill it with sterile saline solution/hypertonic solution (usually with concentration of 4.5%).

3. Measure baseline (pre-salbutamol) FEV_1 (or PEF). Premedicate the subject with inhaled salbutamol (200 μg) and repeat FEV_1 (or PEF) measurement after 10 min.

4. Start nebulisation and ask the subject to perform tidal breathing (set the clock for 15–20 min).

5. Ask the patient to perform inhalation for 5 min intervals followed by coughing and expectoration (the clock should be stopped at each coughing episode). Encourage the subject to cough and spit at any time during the induction if he/she feels the urge to do so.

SPUTUM PROCESSING AND ANALYSIS

Once a sputum sample has been obtained sputum processing should be initiated within two hours in order to avoid significant changes in the number of cells and inflammatory mediators.

The most crucial step of the analytical method is the selection of the sample. Three different techniques of processing have been proposed.

i) Processing the entire expectoration specimen given by the patient without selection.

ii) Selecting all the viscid or denser portion taken from the expectorated sample, which effectively minimizes contamination with saliva.

iii) We used an inverted microscope for better exclusion of saliva and its epithelial cells (this is in practice a modification of technique) . After selection, the sample was put into a polystyrene tube ,

weighing of the tube with the sample, followed by addition of a quantity of 0.1% Dithiothreitol(DTT) solution or its equivalent Dithioerythritol (DTE)× 4 volumes of the weight of the sample, to break the disulphide bonds in the mucin molecules, allowing release of cells17. Subsequently, the sample is agitated on a vortex mixer for about 30 seconds and then placed for homogenization on a tube rocker (3D-Shaker) at 220C for about 20 minutes. An equal volume of phosphate-buffer saline (PBS) solution is then added, to achieve a more efficient dilution of the sample and dispersion of the cells. The sample is agitated again on vortex for about 15seconds and homogenized on the tube rocker for about5 minutes. Sample filtration through a 48 μm nylon mesh was strongly recommended for the removal of remaining mucus and debris. This filtration process, along with the following centrifugation, slightly reduces the total cell count (TCC). Centrifugation at 300-1500×g is continued for about 10 minutes and the emerging supernatant was stored at -70oC. The sediment was used for the estimation of TCC with the use of a haemocytometer (Neubauer) and trypan blue staining. The cell pellet was diluted with PBS to an adjusted concentration of 1.0×106 cells/ml. Finally, cytospin smears are prepared with cytotubes (40-65 μl of the sample in each) and placed for cytocentrifugation at 22×g for 6 minutes [19]. The smears are

stained with Giemsa and May-Grunwald stains, in order to determine the differential cell count (DCC), counting a minimum of 400 nonsquamous cells, and the result is reported as the percentages of macrophages, neutrophils, lymphocytes, eosinophilis and bronchial epithelial cells, among the total nonsquamous cells.

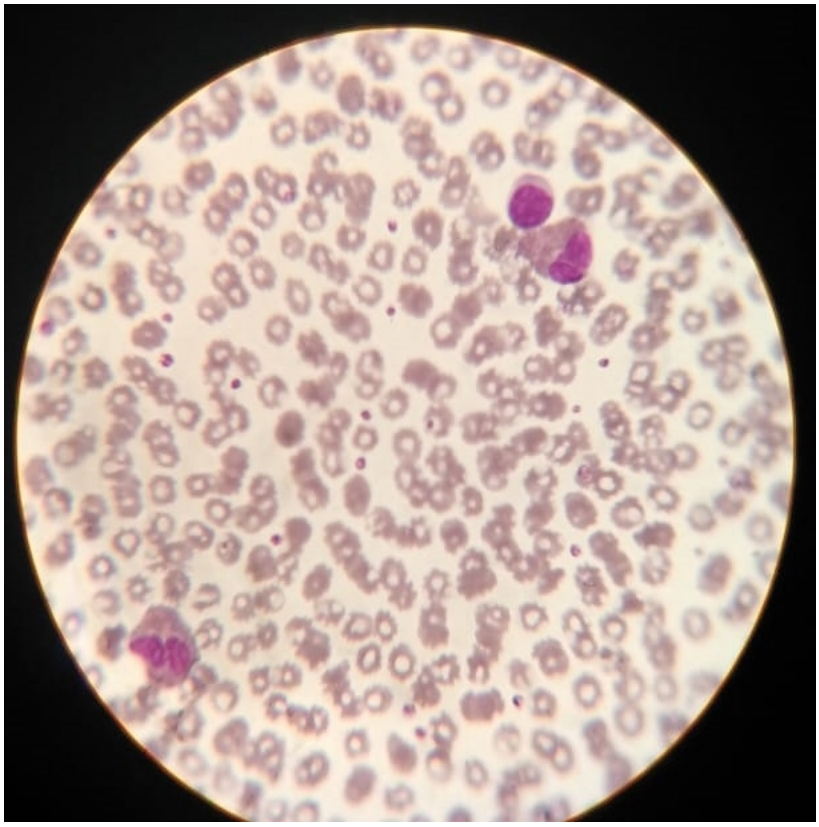
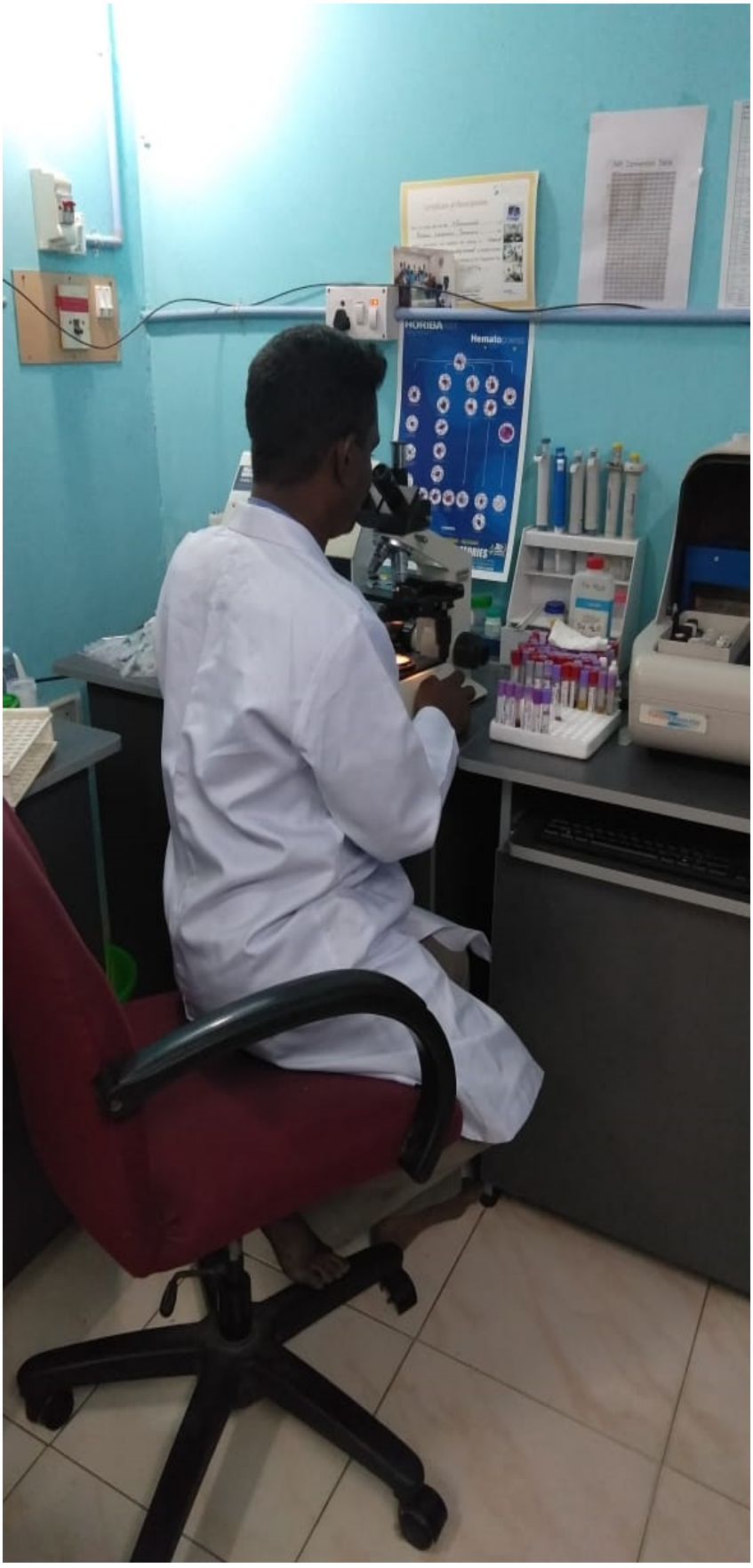


Figure showing eosinophils in light microscope


HORIBA

STEPS IN PERFORMING AN ABSOLUTE EOSINOPHIL COUNT

1. **Drawing Blood** (*drop puncture method):* skin was cleaned , dried and then punctured . With a gauze, wipe away first two drops. As the blood oozes from the wound, draw it into the pipette until slightly past the 0.5 graduation. The pipette was then quickly withdrawn, the tip wiped free of excess blood and lightly touched to draw the blood down to the 0.5 line. Avoided taking blood which was exposed to air for more than a few seconds or showed any clot formation.
2. **Mixing Blood and Diluents:** Immediately after drawing blood, immerse the end of the pipette into the eosinophil diluting fluid and while rotating the pipette between the fingers, draw fluid to the graduation above the bulb. Care should be taken to prevent blood from leaking out of the pipette especially when it is first put into the diluent.
3. **Shaking the Pipette:** The pipette was held between the thumb and forefinger and shaken slowly in a wide arc for approximately 10 seconds. Between each stroke, the pipette was rotated approximately 45 degrees. Care should be taken to close one or both ends of the pipette tightly with the finger to avoid leakage.

4. **Charging the Chamber:** The chambers should be loaded immediately after the pipette was shaken. Hold the pipette at a 45 degree angle, discharge 3 drops of the solution to empty the capillary stem, then place the tip of the pipette on the chamber to be loaded. Allow the fluid to run out rapidly under the cover glass and fill the chamber without overflowing at the edges. The forefinger may be placed over the rear of the pipette to control the rate of flow of the fluid.

5. **Counting Eosinophils:** Allow the loaded counting chamber to stand for at least 3 minutes to permit lysis, staining and settling of the cells. After the cells have settled, the slide may be moved around as desired or it may stand for several hours before counting. Evaporation may be retarded by moistening the inside of a slide box or similar container and inverting it over the slide. Cells are most recognizable and easiest to count at a magnification of 150 times with a field of vision which includes a one square millimeter area. The eosinophils have a distinct cell wall enclosing numerous large red or pink granules. Count the number of eosinophils in the 4 corner squares imder the microscope using a low power objective within 30 minutes. Absolute eosinophil coimt (AEC) = Total number of eosinophils in 4 squares X 25.

6. **Cleaning**: After completing the count, remove the cover glass and clean the counting chamber with water or a mild cleaning solution (10% solution of bleach). Dry the counting chamber with a soft cloth or wipe, or rinse with acetone.

DATA ANALYSIS:

The data were collected and statistical analysis was done using SPSS software Version 21.0. The correlation of sputum eosinophil count, peripheral eosinophil count with severity of asthma was analyzed by Pearson's Chi-square test, Fisher's exact test, and the correlation coefficient was reported together with standard error of the estimate.

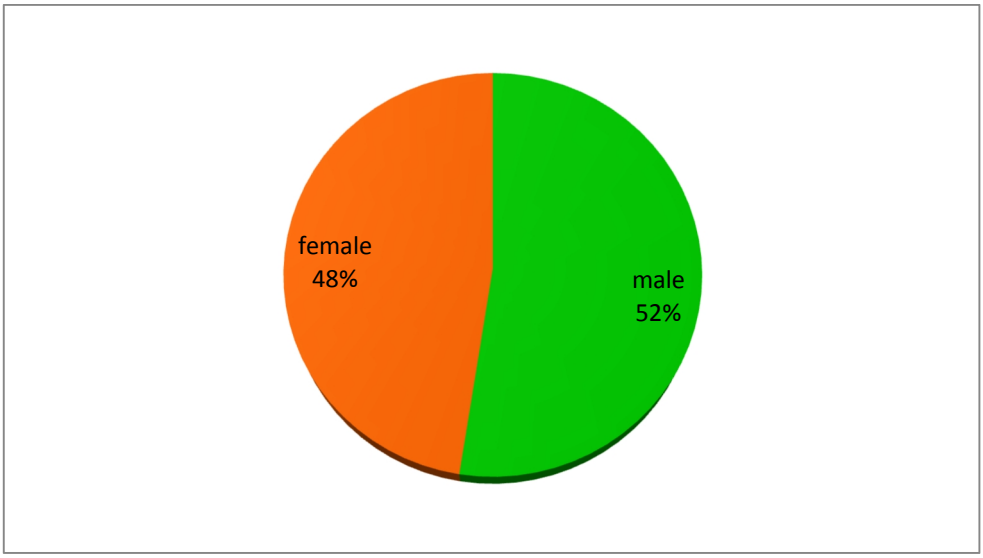
5.RESULTS

GENDER DISTRIBUTION

Table 1: GENDER

GENDER	FREQUENCY	PERCENT
MALE	53	52.5%
FEMALE	48	47.5%
TOTAL	101	100.0%

Chart 1: GENDER

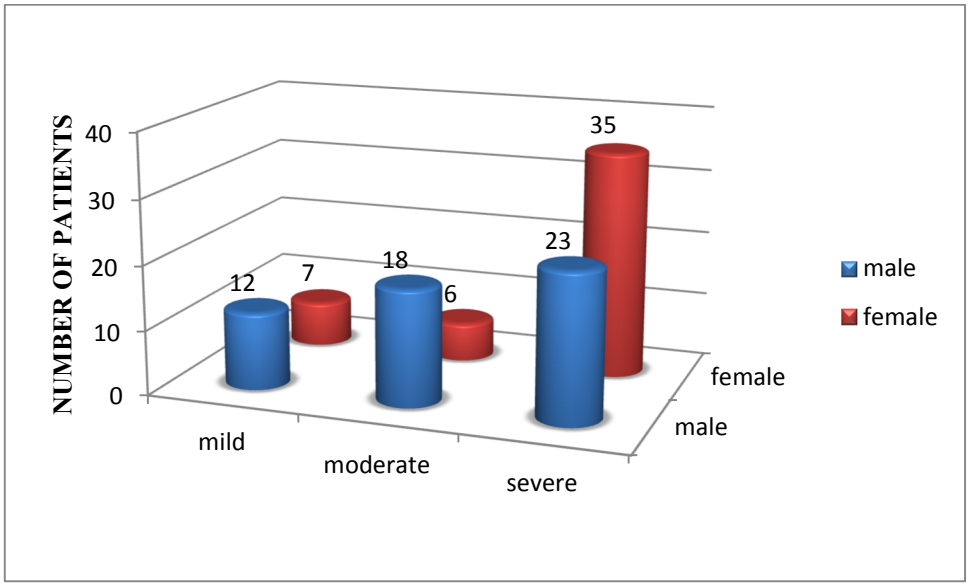


A total of 120 cases underwent initial evaluation, out of which 101 were included in the study and remaining were excluded due to alternative diagnosis. Out of total 101 cases, 52% (n=53) were male and 48% (n=48) were female.

Table 2: CORRELATION OF GENDER AND SEVERITY OF ASTHMA

GENDER	SEVERITY MILD	%	MODERATE	%	SEVERE	%	P VALUE
MALE	12	22.64%	18	33.96%	23	43.40%	0.008
FEMALE	7	14.58%	6	12.50%	35	72.92%	
TOTAL	19		24		58		

Chart 2: CORRELATION OF GENDER AND SEVERITY OF ASTHMA

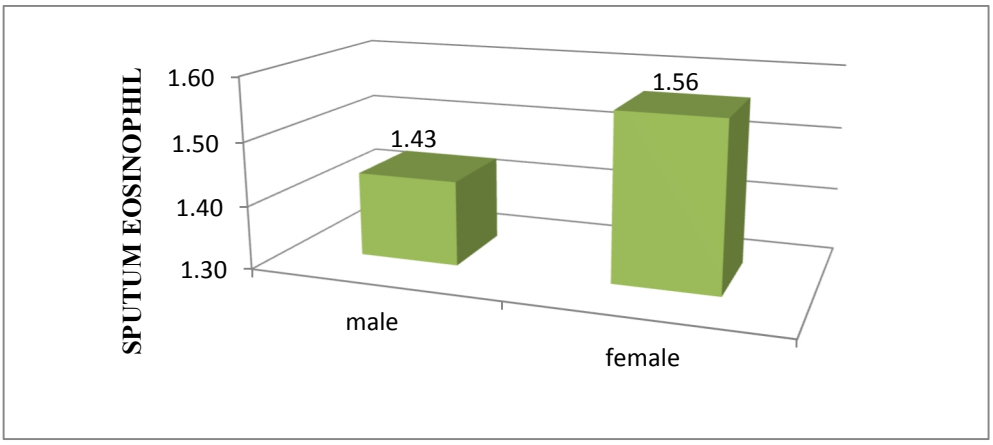


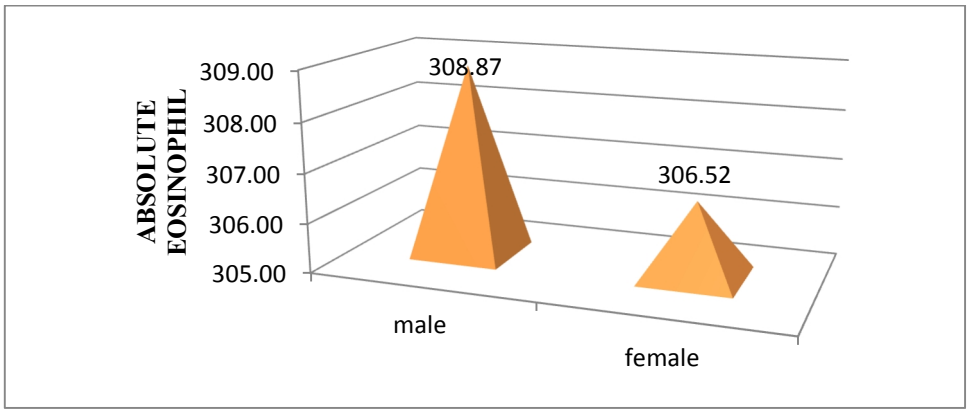
Gender was compared with severity of bronchial asthma and found that most of the females were presented with severe asthma when compared to males showing significant correlation with p value of 0.008

Table 3: CORRELATION OF GENDER AND EOSINOPHIL COUNT

GENDER		N	MEAN	STD. DEVIATION	P VALUE
SPUTUM EOSINOPHIL	MALE	53	1.43	1.22	0.576
	FEMALE	48	1.56	1.07	
ABSOLUTE EOSINOPHIL	MALE	53	308.87	175.85	0.943
	FEMALE	48	306.52	152.34	

Chart 3 & 4 : CORRELATION OF GENDER AND EOSINOPHIL COUNT





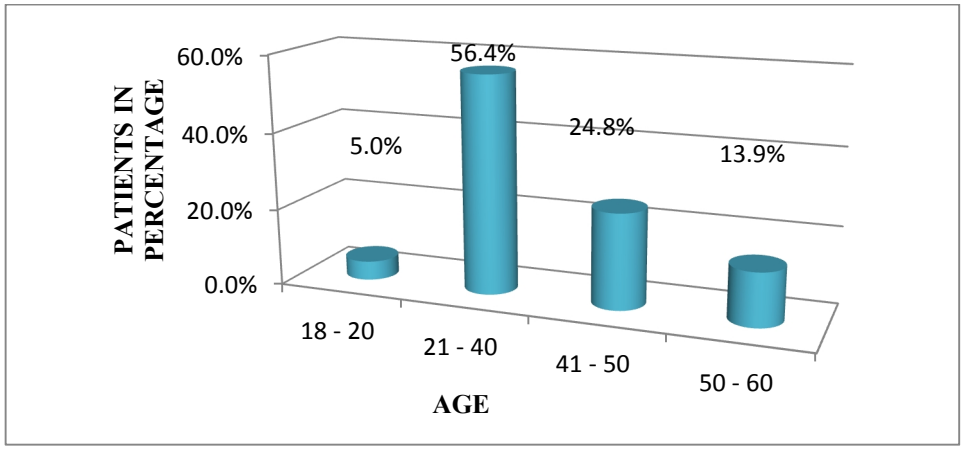
Gender was compared with sputum and absolute eosinophil showing no significant correlation (p value of 0.576 and 0.943.).

AGE DISTRIBUTION

Table 4: AGE DISTRIBUTION

AGE	FREQUENCY	PERCENT
18 - 20	5	5.0%
21 - 40	57	56.4%
41 - 50	25	24.8%
50 - 60	14	13.9%
TOTAL	101	100.0%

Chart 5: AGE DISTRIBUTION



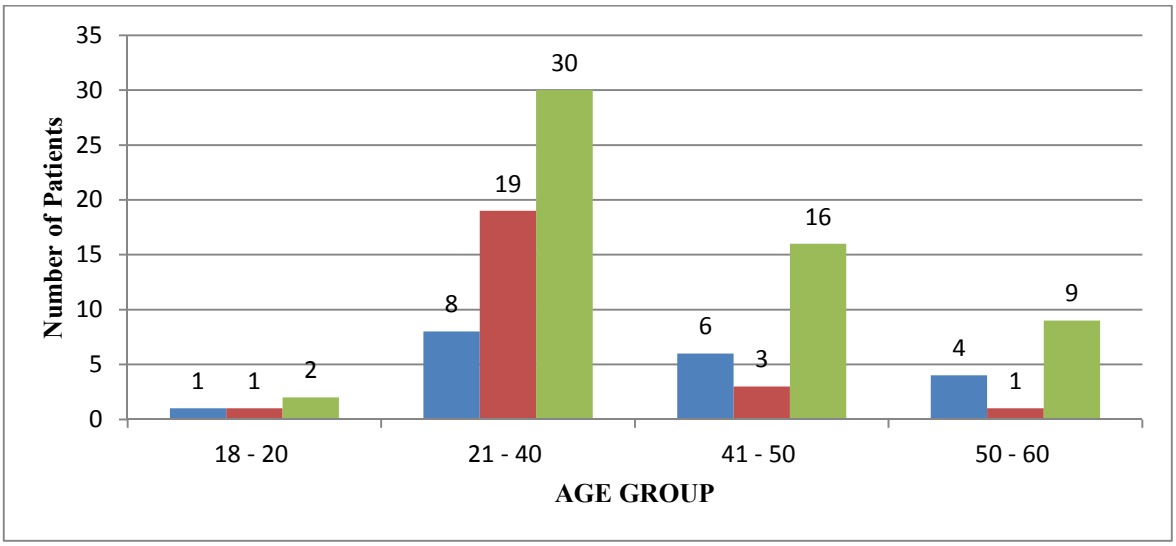
The distribution of age varied from 20 to 60 years. The overall mean age ofthe study subject was 39 years. Maximum patients were found in the 21to 40 years age group (56.4 %, n= 57) followed by more than 41 to 50 years age group (24.8%, n=25) and least in less than 20 years (5%, n=5).

CORRELATION OF AGE GROUP WITH SEVERITY OF ASTHMA

Table 5: CORRELATION OF AGE GROUP WITH SEVERITY OF ASTHMA

		SEVERITY			P
		MILD	MODERATE	SEVERE	VALUE
AGE GROUP	18 - 20	1	1	2	0.529
	21 - 40	8	19	30	
	41 - 50	6	3	16	
	50 - 60	4	1	9	
TOTAL		19	24	58	

Chart 6: CORRELATION OF AGE GROUP WITH SEVERITY OF ASTHMA



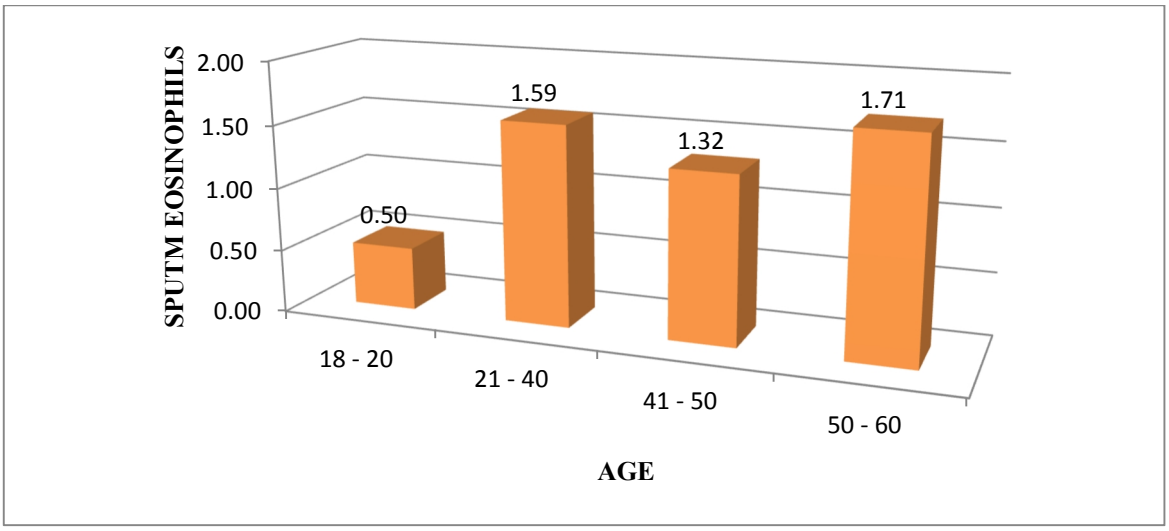
Age group was compared with severity of bronchial asthma showing no significant correlation (p value of 0.529.)

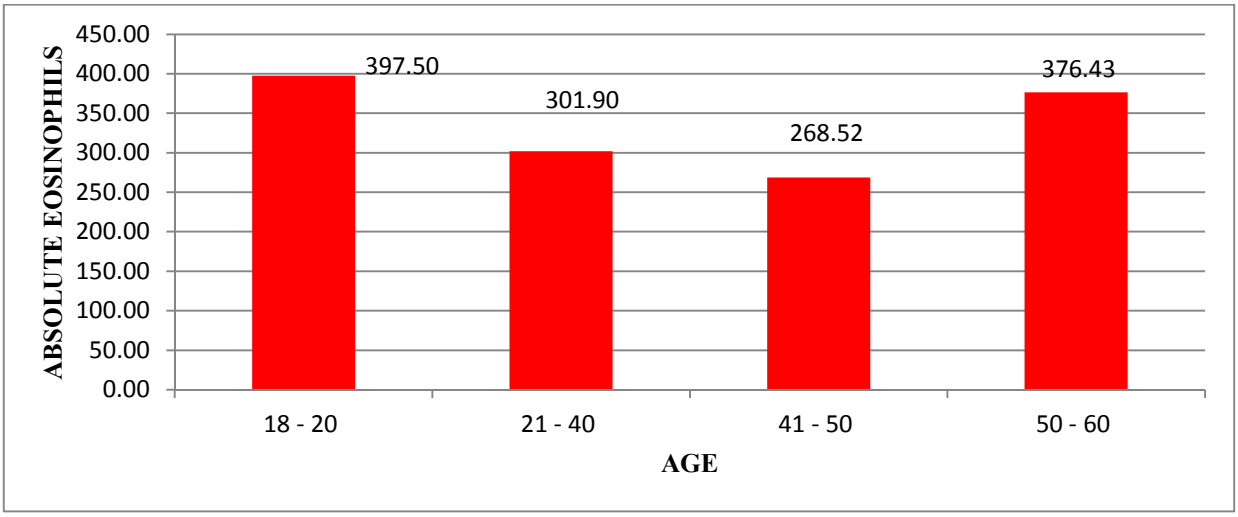
CORRELATION OF AGE GROUP WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

Table 6 : CORRELATION OF AGE GROUP WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

AGE GROUP		N	MEAN	STD. DEVIATION	P VALUE
SPUTUM EOSINOPHIL	18 - 20	4	0.50	1.00	0.215
	21 - 40	58	1.59	1.11	
	41 - 50	25	1.32	1.03	
	50 - 60	14	1.71	1.44	
	TOTAL	101	1.50	1.15	
ABSOLUTE EOSINOPHIL	18 - 20	4	397.50	274.76	0.162
	21 - 40	58	301.90	128.26	
	41 - 50	25	268.52	95.41	
	50 - 60	14	376.43	300.96	
	TOTAL	101	307.75	164.28	

Chart 7 & 8 : CORRELATION OF AGE GROUP WITH SPUTUM EOSINOPHIL



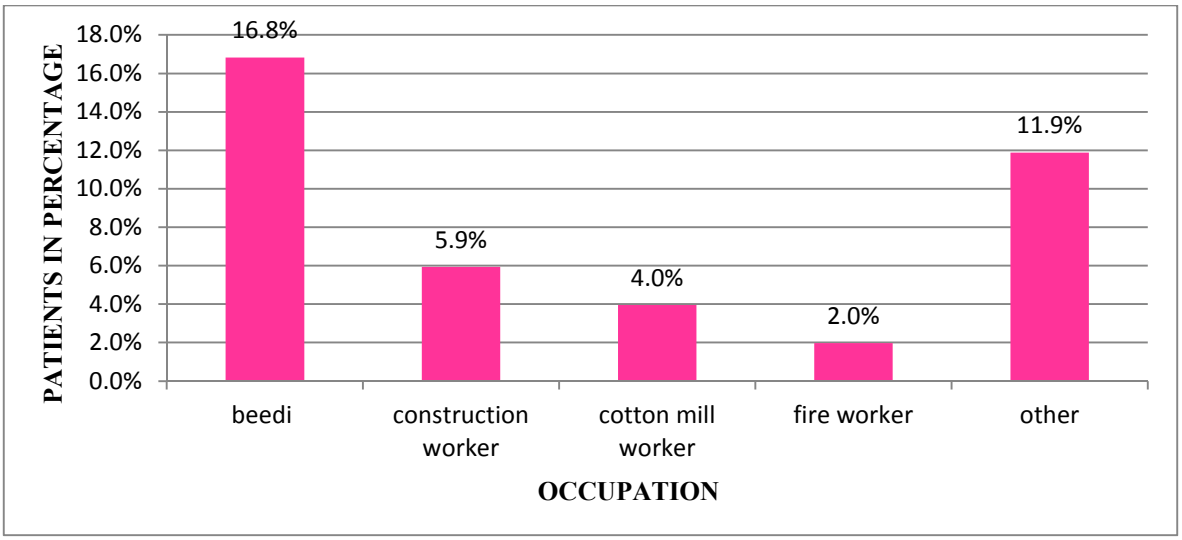


Age group was compared with sputum and absolute eosinophil count showing no significant correlation with p value of 0.215 and 0.162.

Table 7 : OCCUPATION

OCCUPATION	FREQUENCY	PERCENT
	60	59.4
Beedi worker	17	16.8%
Construction worker	6	5.9%
Cotton mill worker	4	4.0%
Fire worker	2	2.0%
Other	12	11.9%
Total	101	100.0%

Chart 9: OCCUPATION



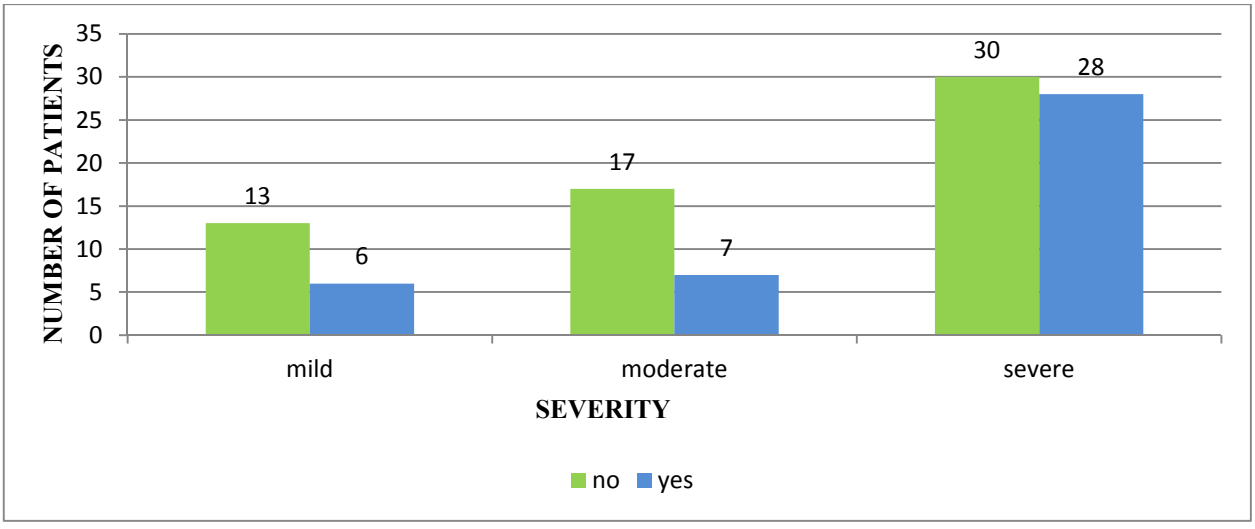
In our study , 59.4 % cases were exposed to occupation related risk factor among them 16.8% were beedi worker .

CORRELATION OF ENVIRONMENT EXPOSURE WITH SEVERITY OF ASTHMA

Table 8 : CORRELATION OF ENVIRONMENT EXPOSURE WITH SEVERITY OF ASTHMA

		SEVERITY			P VALUE
		MILD	MODERATE	SEVERE	
ENVIRONMENT	NO	13	17	30	0.186
	YES	6	7	28	
TOTAL		19	24	58	

Chart 10: CORRELATION OF ENVIRONMENT EXPOSURE WITH SEVERITY OF ASTHMA



Patient who had an environmental exposure history (n = 41) correlated with severity of asthma showed no significant correlation (p value 0.186).

CORRELATION OF ENVIRONMENT EXPOSURE WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

Table 9 : CORRELATION OF ENVIRONMENT EXPOSURE WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

ENVIRONMENT		N	MEAN	STD. DEVIATION	P VALUE
SPUTUM EOSINOPHIL	NO	60	1.32	0.98	0.058
	YES	41	1.76	1.32	
ABSOLUTE EOSINOPHIL	NO	60	295.00	167.14	0.348
	YES	41	326.41	160.20	

Chart 11: CORRELATION OF ENVIRONMENTAL EXPOSURE WITH SPUTUM EOSINOPHIL

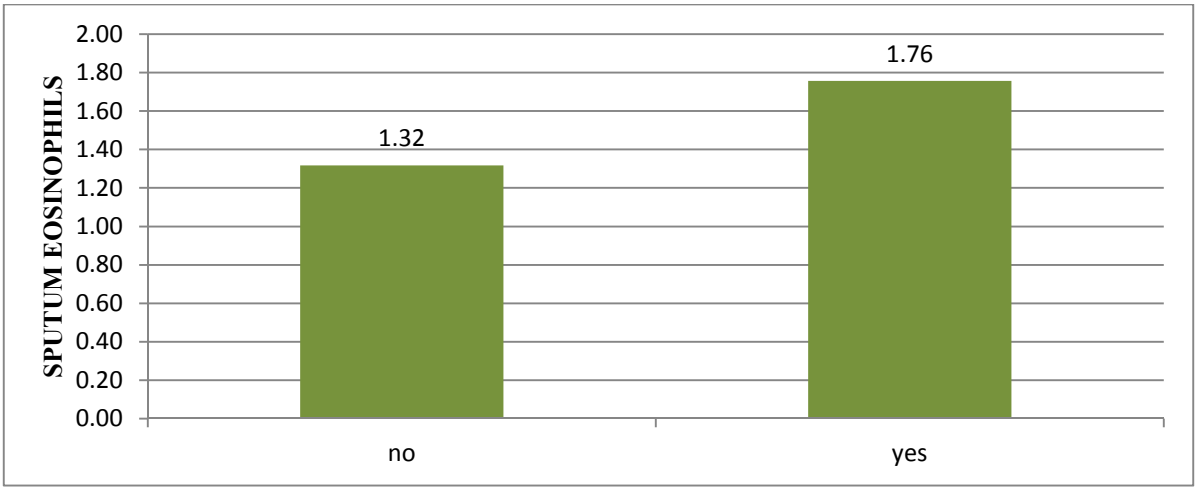
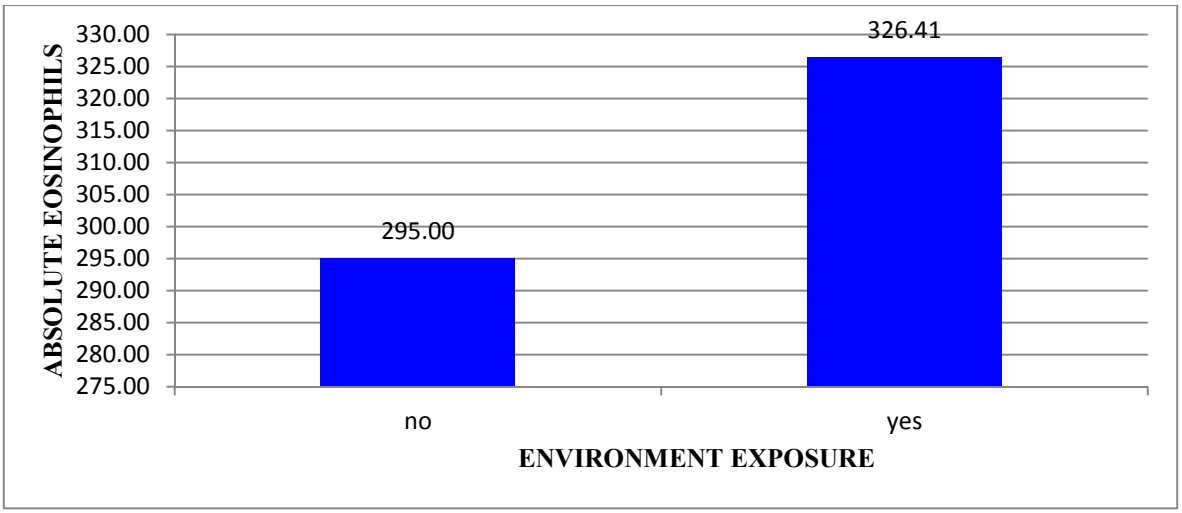


Chart 12: CORRELATION OF ENVIRONMENTAL EXPOSURE WITH ABSOLUTE EOSINOPHIL



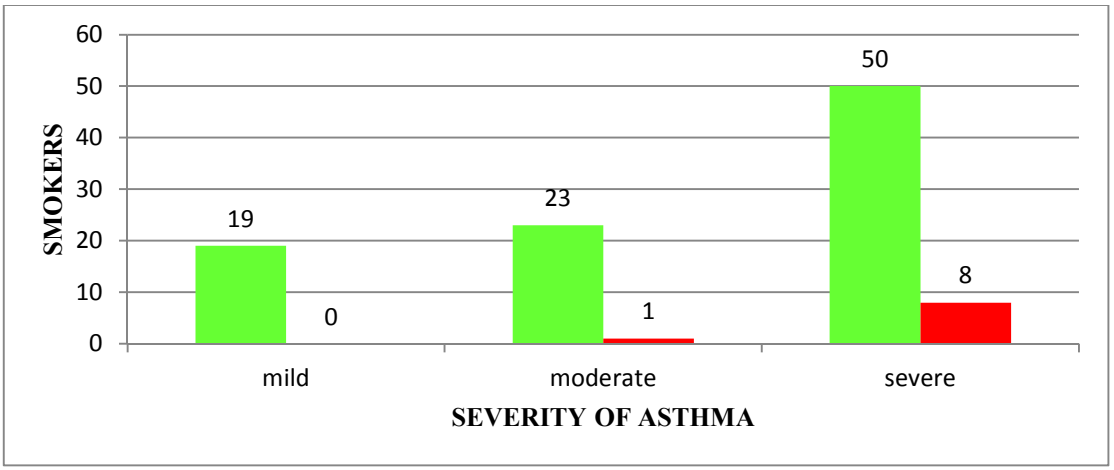
There was no significant correlation between the environmental exposure and eosinophil count (p value 0.058 and 0.348).

SMOKERS

Table 10 : Smokers

		SEVERITY		
		MILD	**MODERATE**	**SEVERE**
SMOKER	NO	19	23	50
	yes	0	1	8

Chart 13: Smoker



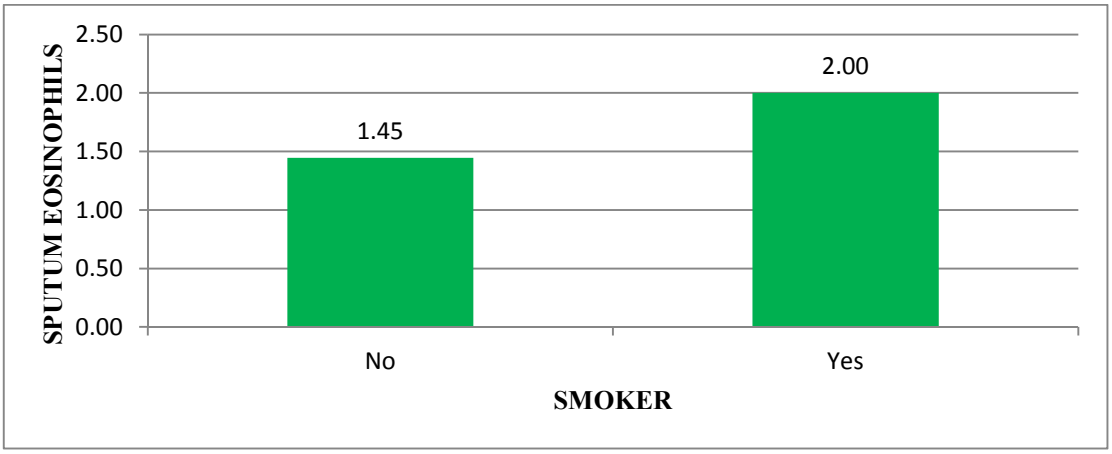
Total 9 Smokers in our study, out of them 8 were severe asthmatics.

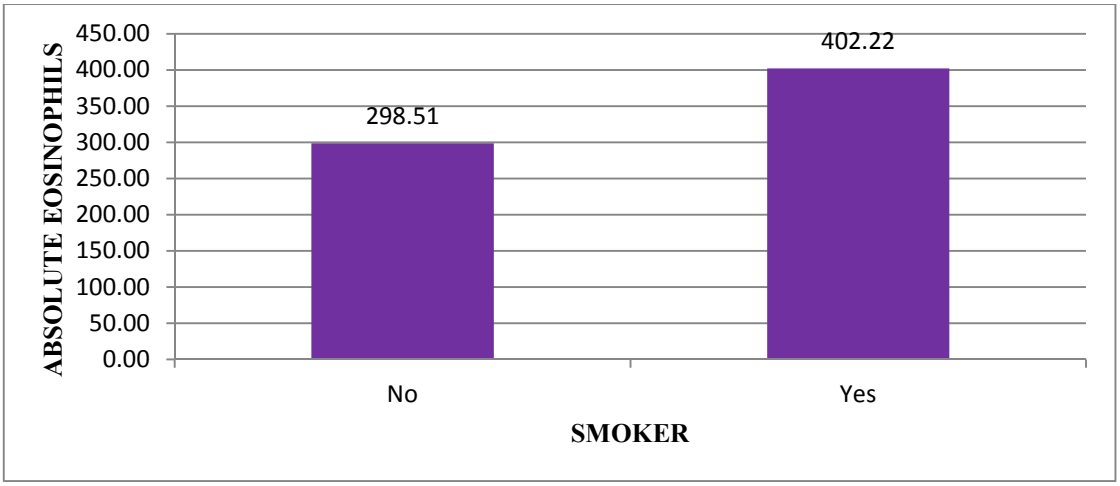
CORRELATION OF SMOKERS WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

Table 11: CORRELATION OF SMOKERS WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

SMOKER		N	MEAN	STD. DEVIATION	P VALUE
SPUTUM EOSINOPHIL	NO	92	1.45	1.14	0.167
	YES	9	2.00	1.12	
ABSOLUTE EOSINOPHIL	NO	92	298.51	148.74	0.070
	YES	9	402.22	273.26	

Chart 14 & 15: CORRELATION OF SMOKERS WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT





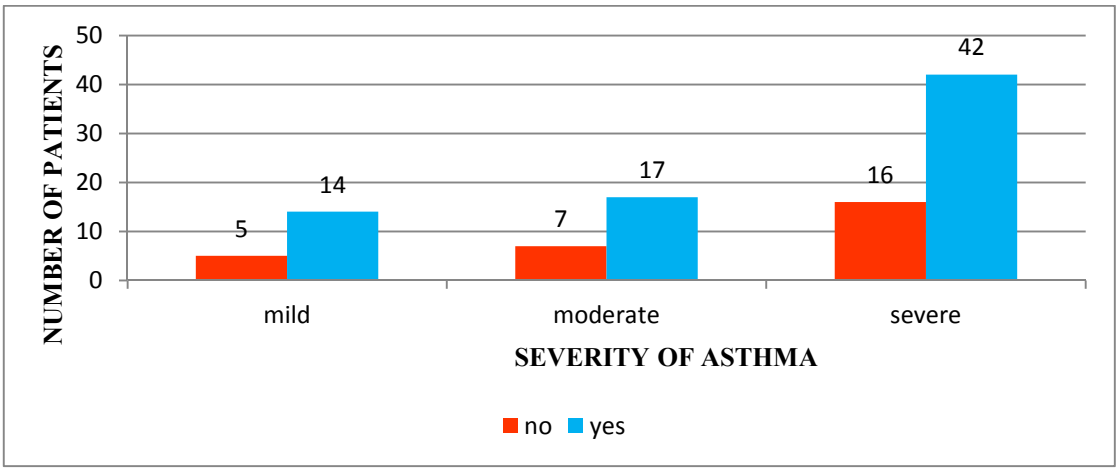
Smokers were correlated with sputum and absolute eosinophil count showed no significant correlation with p value of 0.167 and 0.070.

FAMILY HISTORY OF ASTHMA

Table 12: FAMILY HISTORY OF ASTHMA

		SEVERITY		
		MILD	MODERATE	SEVERE
FAMILY HISTORY	NO	5	7	16
	yes	14	17	42
Total		19	24	58

Chart 16: FAMILY HISTORY OF ASTHMA



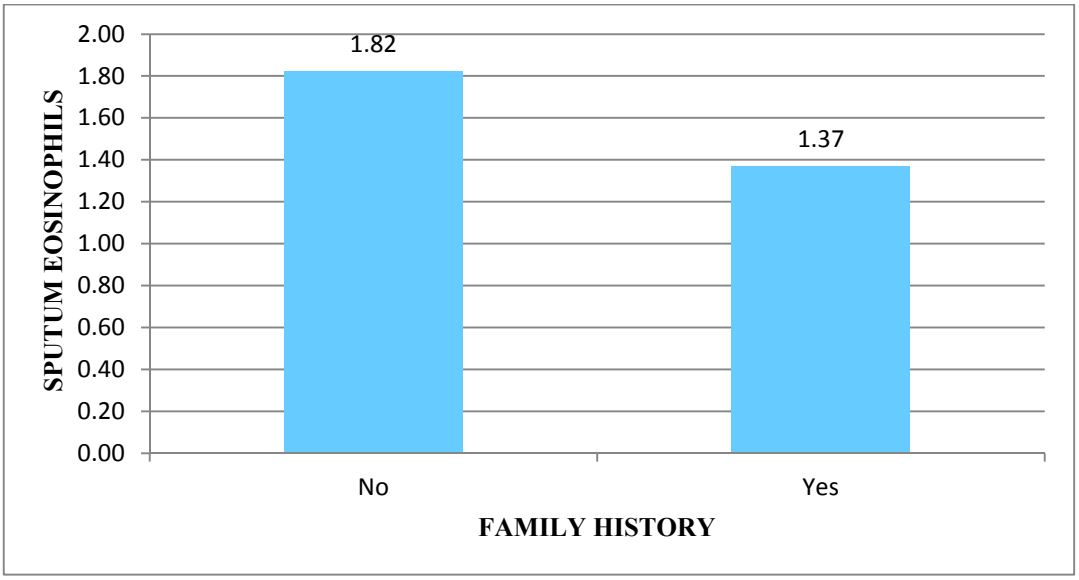
Out of 101 cases , 73 cases had a family history of asthma and most of them were severe asthmatics.

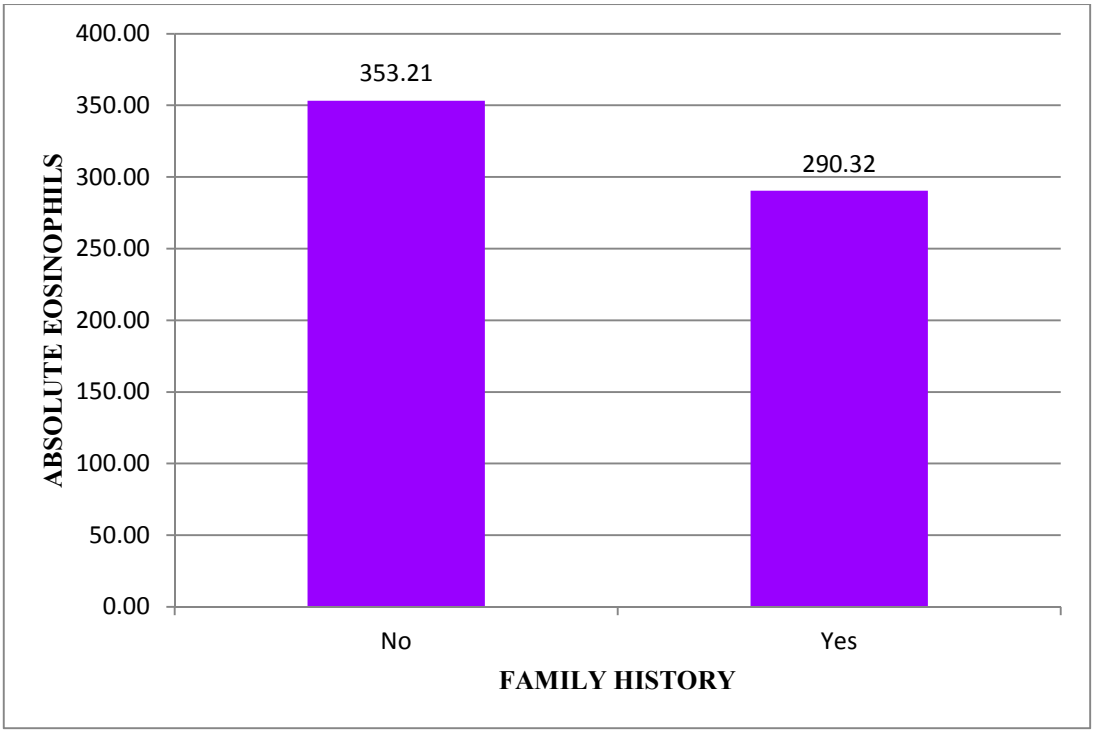
CORRELATION OF FAMILY HISTORY CASES WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

Table 13: CORRELATION OF FAMILY HISTORY CASES WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

FAMILY HISTORY		N	MEAN	STD. DEVIATION	P VALUE
SPUTUM EOSINOPHIL	NO	28	1.82	1.31	0.076
	YES	73	1.37	1.06	
ABSOLUTE EOSINOPHIL	NO	28	353.21	192.99	0.085
	YES	73	290.32	149.68	

Chart 17 & 18: CORRELATION OF FAMILY HISTORY CASES WITH SPUTUM AND ABSOLUTE EOSINOPHIL COUNT





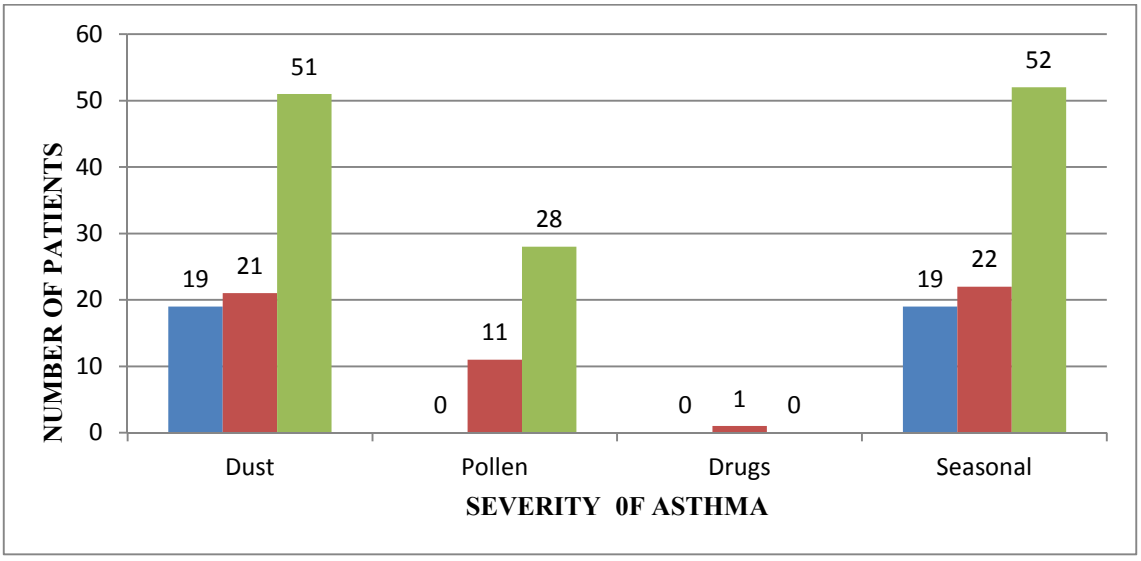
There was no significant correlation between the family history and eosinophil count.

ALLERGENS

Table 14: ALLERGENS

ALLERGIES	SEVERITY			P VALUE
	MILD	MODERATE	SEVERE	
DUST	19	21	51	0.276
POLLEN	0	11	28	0.001
DRUGS	0	1	0	0.198
SEASONAL	19	22	52	0.349

Chart 19: ALLERGENS



Among 101 cases, dust and seasonal allergens were the most common triggering factors. Allergens were correlated with severity of asthma, showed no significant correlation except pollen with p value of 0.001.

CORRELATION OF DURATION 0F SYMPTOMSM ,SEVERITY AND EOSINOPHIL COUNT

Table 15: CORRELATION OF DURATION 0F SYMPTOMSM ,SEVERITY AND EOSINOPHIL COUNT

		SEVERITY	FEV1	SPUT_EOS	ABSO_EOS
COUGH DURATION	PEARSON CORRELATION	.427**	-.433**	.214*	.165
	P VALUE	.000	.000	.031	.099
EXPECTORATION DURATION	PEARSON CORRELATION	.427**	-.433**	.214*	.165
	P VALUE	.000	.000	.031	.099
WHEEZE DURATION	PEARSON CORRELATION	.383**	-.391**	.172	.172
	P VALUE	.000	.000	.085	.085
DYSPNEA DURATION	PEARSON CORRELATION	.427**	-.433**	.214*	.165
	P VALUE	.000	.000	.031	.099

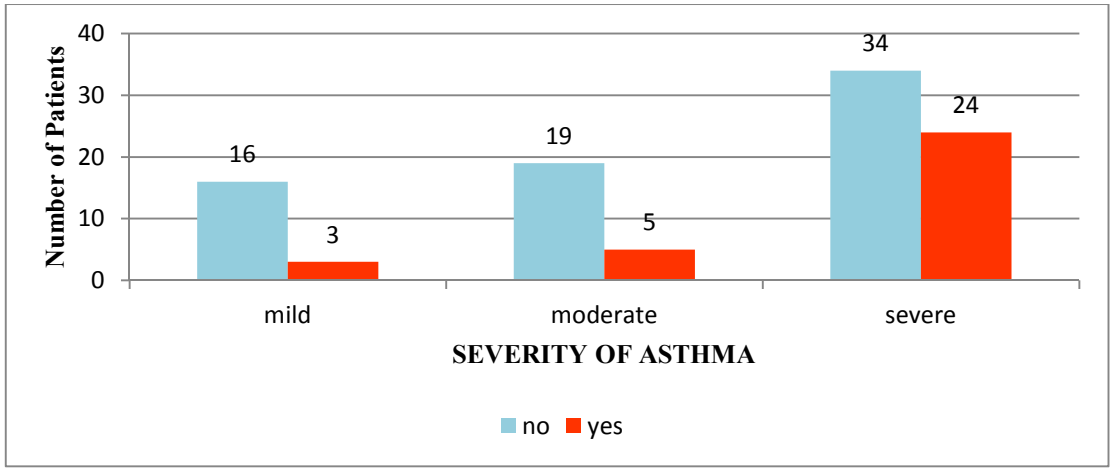
Duration of symptoms was compared with severity, fev1 and eosinophil count showed significant correlation. Duration of symptoms showed direct correlation to severity of asthma, eosinophil count and inverse correlation to FEV1.

CORRELATION OF CO-MORBIDITIES OF ASTHMA WITH SEVERITY OF ASTHMA

Table 16: CORRELATION OF CO-MORBIDITIES OF ASTHMA WITH SEVERITY OF ASTHMA

CO-MORBIDITIES	SEVERITY			P VALUE
	MILD	MODERATE	SEVERE	
DEPRESSION	2	2	3	.694
OSA	0	0	2	.469
GERD	4	3	8	.693
RHINOSINUSITIS	3	5	24	.04

Chart 20: CORRELATION OF CO-MORBIDITIES OF ASTHMA WITH SEVERITY OF ASTHMA



Rhinosinusitis was the common co-morbidity of asthma in our study (n = 32)showed a significant correlation with severity of asthma (p value 0 .04)

BMI

Table 17: CORRELATION BETWEEN BMI AND SEVERITY

		severity
BMI	Correlation Coefficient	.031
	P value	.696

Table 18: CORRELATIONS OF BMI AND EOSINOPHIL COUNT

		SPUTUM EOSINOPHIL	**ABSOLUTE EOSINOPHIL**
BMI	**PEARSON CORRELATION**	.008	-.066
	P VALUE	.937	.515

There was no significant correlation between BMI , severity and eosinophil count.

Table 19: FORCED VITAL CAPACITY (FEV1)

		SPUTUM EOSINOPHIL	ABSOLUTE EOSINOPHIL
FEV1	PEARSON CORRELATION	-.532**	-.333**
	P VALUE	.000	.001

There is an inverse correlation between FEV1 and eosinophil count

Table 20: CORRELATION BETWEEN SPUTUM AND ABSOLUTE EOSINOPHIL COUNT

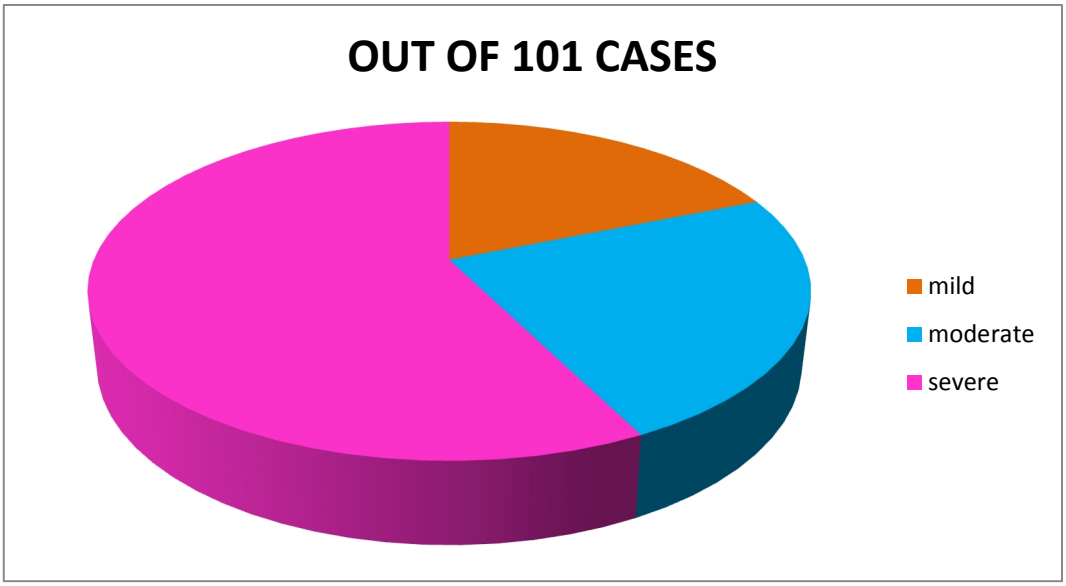
		SUM OF SQUARES	DF	MEAN SQUARE	F	SIG.
SPUTUM EOSINOPHIL	BETWEEN GROUPS	36.740	2	18.370	19.049	.000
	WITHIN GROUPS	94.508	98	.964		
	TOTAL	131.248	100			
ABSOLUTE EOSINOPHIL	BETWEEN GROUPS	301140.191	2	150570.095	6.154	.003
	WITHIN GROUPS	2397718.621	98	24466.517		
	TOTAL	2698858.812	100			

There was significant correlation between sputum and absolute eosinophil.

Table 21: SEVERITY OF ASTHMA

SEVERITY	OUT OF 101 CASES
MILD	19
MODERATE	24
SEVERE	58

Chart 21: SEVERITY OF ASTHMA

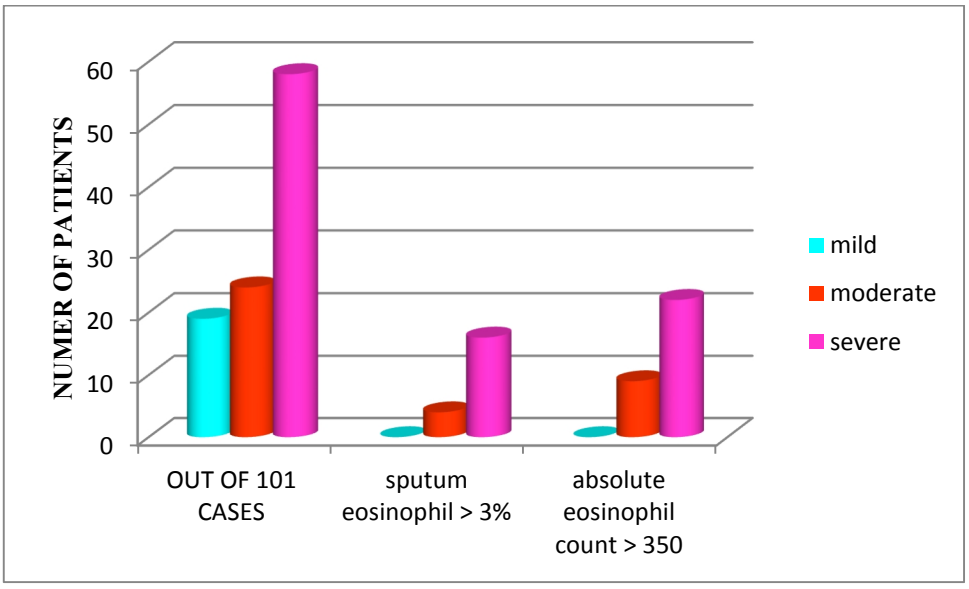


In our study, according to GINA guidelines severity of asthma cases were categorized. Out of 101 case, 19 of them mild, 24 of them moderate and 58 of them severe.

Table 22: SEVERITY OF ASTHMA AND EOSINOPHIL COUNT

SEVERITY	OUT OF 101 CASES	SPUTUM EOSINOPHIL > 3%	ABSOLUTE EOSINOPHIL COUNT > 350
mild	19	0	0
moderate	24	4	9
severe	58	16(27.6%)	22(30.5%)

Chart 22: SEVERITY OF ASTHMA AND EOSINOPHIL COUNT

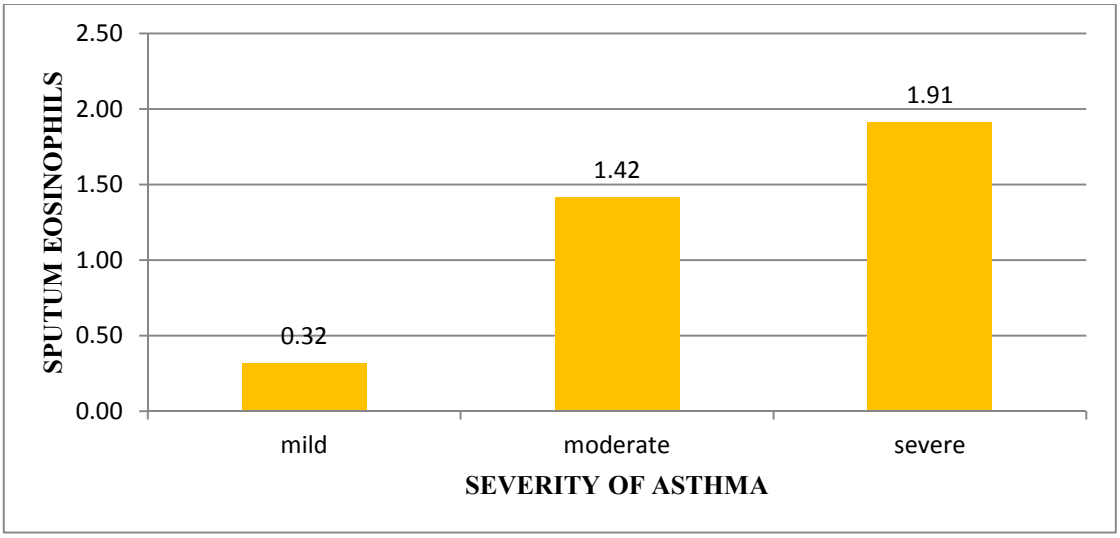


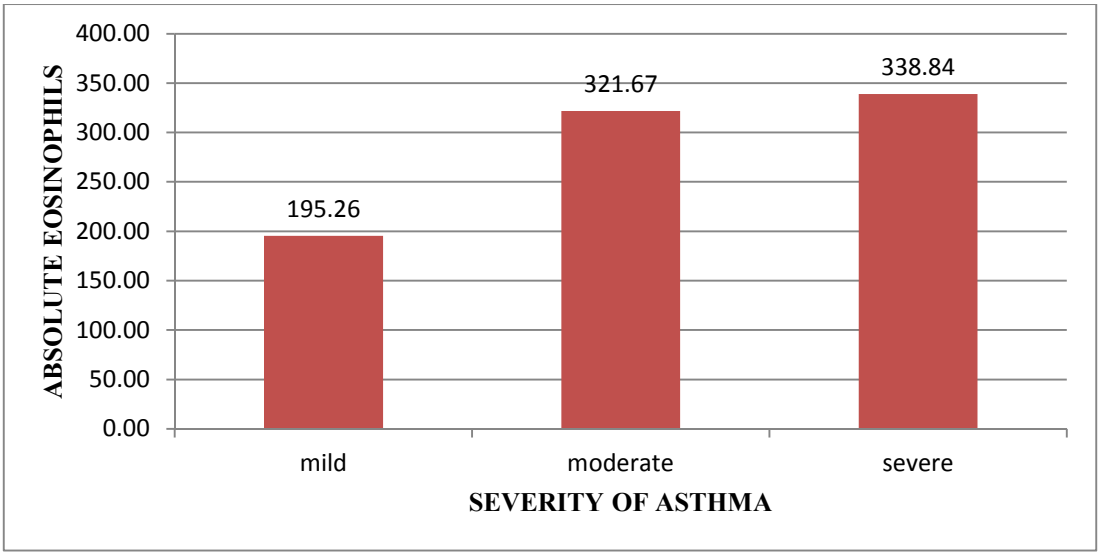
Total number of cases showing sputum eosinophils more than 3% was 20, out of them 16 were present in severe asthmatics (27.6%). Total number of cases showing absolute eosinophils more than 350 was 31 ,out of them 22 were present in severe asthmatics (30.5 %).

Table 23: CORRELATION OF SEVERITY AND EOSINOPHIL COUNT

DEPENDENT VARIABLE			MEAN DIFFERENCE (I-J)	STD. ERROR	SIG.
SPUTUM EOSINOPHIL	MILD	MODERATE	-1.10088*	.30156	.001
		SEVERE	-1.59800*	.25958	.000
	MODERATE	MILD	1.10088*	.30156	.001
		SEVERE	-.49713	.23835	.119
	SEVERE	MILD	1.59800*	.25958	.000
		MODERATE	.49713	.23835	.119
ABSOLUTE EOSINOPHIL	MILD	MODERATE	-126.40351*	48.03280	.030
		SEVERE	-143.58167*	41.34668	.002
	MODERATE	MILD	126.40351*	48.03280	.030
		SEVERE	-17.17816	37.96412	1.000
	SEVERE	MILD	143.58167*	41.34668	.002
		MODERATE	17.17816	37.96412	1.000

Chart 23 & 24: CORRELATION OF SEVERITY AND EOSINOPHIL COUNT





Severity of asthma correlated with the sputum and blood eosinophil count and showed a significant correlation.

6. DISCUSSION

In our study, total 101 cases were selected, out of them 52% (n=53) were male and 48% (n=48) were female. According to 2012 census (INSEARCH), in India prevalence of asthma is 2.05 % with almost equal sex proportion of male 1.09% and female 0.96%. In United States of America, asthma prevalence was higher among children (9.3%) than adults (8.0%). Overall, females (9.5%) were more than males (7.0%). Although the female-to-male balance changes over development, with asthma less common in females than males during childhood, but more common in females than males during adulthood because of hormonal factors. [95]

Gender were compared with severity of bronchial asthma and found that most of the females were presented with severe asthma when compared to males showing significant correlation (p value 0.008). In various literatures, asthma in women was reported to be more severe and associated with higher health care use [100, 101]. After puberty, a gender switch occurs, and asthma becomes more prevalent and severe in women [96, 97, 98]. Girls who mature early, and pregnant women are likely to be exposed to higher estrogen levels, and greater cumulative hormonal exposure of sex hormones, which place them at higher risk for asthma development later in life. In contrast, oral contraceptive may be protective and decrease the risk of exacerbation in asthmatic women [99].

In our study, the distribution of age varied from 20 to 60 years. The overall mean age was 39 years. Maximum patients were found in the 21 to 40 years' age group (56.4 %, n= 57) followed by more than 41 to 50 years age group (24.8%, n=25) and least in less than 20 years (5%, n=5). In most of the studies, common age group prevalence in adult population is between 18 to 40. Asthma is more common in children in the 5 to 14 years age group. Being a chronic disease, the cumulative prevalence of asthma increases as the age advances.

We found 59.4 % cases were exposed to occupation related risk factor, among them 16.8% were beedi workers. According to literatures, a systematic analysis of population attributable risk showed that an estimated 16.3% of all cases of adult-onset asthma are caused by occupational exposure [102].There was discrepancy between the rates of asthma diagnosed by a health professional as being work related (4.7% of all new asthma cases) and rates that include self-reported cases of work-related asthma (18.2% of all new asthma cases)[103] .

In our study we found that there was no significant correlation between the environmental exposure population group , severity and eosinophil count According to literatures, occupational asthma can be separated into eosinophilic and noneosinophilic pathophysiological variants . Among them noneosinophil variant were predominant. Both groups had evidence of sputum neutrophilia. Sputum eosinophilia was

associated with more severe disease and greater bronchodilator reversibility, but no difference in peak expiratory flow response to work exposure. So the outcome of our study was similar to previous literatures.

In our study , cases who had a family history , smokers , most of them were severe persistent asthmatics and there was no significant correlation to eosinophil count . In literatures, tobacco Smoking was another important cause of increased asthma morbidity among both children and adults.[53-55]. Usually among smokers of non eosinophilic variant, asthma was severe and there was poor response to steroids.

Dust and seasonal allergens are the most common triggering factors in our study. Allergens were correlated with severity of asthma showing no significant correlation except pollen with p value of 0.001. Countries with high air pollution like India, inhaled substance particle are the strongest risk / triggering factor in developing asthma.

Duration of symptoms showed direct correlation to severity of asthma , eosinophil count and inverse correlation to FEV1. It indicated that patients with long duration of symptoms who are not on treatment ,poor compliance , continuous exposure to triggering factors usually present with severe persistent asthma with FEV1 < 60 , frequent exacerbation and increase in eosinophil count.

Rhinosinusitis was the common co-morbidity of asthma in our study (n = 32)showed a significant correlation with severity of asthma (p value .04) .Currently, the prevalence of allergic rhinitis worldwide is between 20 and 30 %, increased from approximately 10–15 % at the midpoint of the twentieth century. According to literatures,10-40% of patients with allergic rhinitis have asthma, the majority of patients with asthma (70-90%) have allergic rhinits and it is the major risk factor for poor asthma control.

Correlation of sputum eosinophil count and severity of asthma

In our study, we found higher percentage of sputum eosinophil count in 20% cases of the study population that included predominantly moderate and severe persistent asthma. We observed most of the studies reported almost similar distribution. We observed high sputum eosinophil count (>3%) was significantly seen in more patients with severe persistent asthma (27.6%) though more than half of them had normal sputum eosniophils. Similar results were observed in various studies.[104-108] . In our study, there was no significant difference in sputum eosinophil level in mild and moderate persistent asthma, and we did not observe a dose–response relationship between asthma severity and proportion of patients with higher sputum eosinophilia, suggesting an asthma phenotype with sputum eosinophilia which may be seen in any asthma severity. Various authors also have reported similar findings. [111,20]. The importance of identifying this phenotype of asthma with elevated sputum eosinophilia

could be related to steroid responsiveness and future studies may demonstrate in the Indian population. In our present study, though there was a significant inverse correlation between sputum eosinophil count and predicted forced expiratory volume in 1 s (P = 0.000) and predicted FVC (P = 0.001), the correlation has been weak. Various studies have also reported significant correlation between sputum eosinophil count and predicted FEV1 (P < 0.05).[111,112-116]

Correlation of absolute eosinophil count and severity of asthma

In our study, we observed increased absolute eosinophil count in 30.5% of the study population that included predominantly moderate and severe persistent asthma similar to sputum eosinophil. We observed high absolute eosinophil count (>350) was significantly seen in more patients with severe persistent asthma (39.9%) though more than half of them had normal absolute eosniophils. Similar results were observed in various studies.[104-108].The results were contradictory with the observation made by Palomino et al [110] . We observed no correlation between absolute eosinophil levels in mild and moderate persistent asthma, there was a significant inverse correlation between FEV1 and absolute eosinophil.

Correlation of sputum eosinophil count and absolute eosinophil count

We found a significant association between absolute eosinophil count and sputum eosinophil count. Only limited studies available between correlation of sputum and absolute eosinophil among them khadadah et al [42] study reported positive correlation between total blood eosinophil counts and eosinophilic cationic protein.

7. SUMMARY

Present study was done to correlate induced sputum eosinophil and absolute eosinophil counts in assessing the clinical severity of bronchial asthma. In our study of 101 asthmatics were selected , out of them 58% patients had severe asthma, 24% patients had moderate asthma, and 19% patients had mild asthma . In our study, prevalence of asthma is more in middle age group with equal sex ratio .dust and seasonal allergens are the most common triggering factors. Beedi workers were more when compared to other occupations. In our study, risk factors for severe asthma was female sex , environment dust exposure, smoking, who had a positive family history of asthma , long duration of symptoms and rhinosinusitis co-morbidity. There was a significant correlation of induced sputum eosinophil and absolute eosinophil count with severe persistent asthma.

8. CONCLUSION

Assessment of eosinophil count in sputum and blood are simple and inexpensive method that can show a direct measurement of airway inflammation. Thus it can help to identify specific phenotypes in asthmatic patients who are more responsive to steroids, which needs to be demonstrated in future studies. It could be the preferred method in routine practice in monitoring airway inflammation and guiding management.

9. LIMITATION

(1) Normal age matched controls from the general population were not included in the study.

(2) Phenotypes of asthma other than eosinophilic were not evaluated.

(3) An increased level of eosinophila was not evaluated further for parasitic infestation.

(4) Assessments for allergic bronchopulmonary aspergillosis were not done

(5) Equal numbers of patients were not recruited in the three groups of asthma severity. Very small numbers in mild asthma influenced our ability to compare across groups for a dose–response relationship.

(6) Follow-up of the patients after steroid therapy was not done.

(7) Repeatability of sputum eosinophils was not assessed.

10. BIBILIOGRAPHY

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PROFORMA

1. NAME :
2. Age :
3. Sex : Male / Female
4. Place of residence :
5. Occupation history :
6. Environmental history :
7. Personal history : SMOKER /NON SMOKER
8. Family history :
9. Allergic history :
10. URT symptoms : sneezing /nasal congestion /headache/runny nose/sore throat
11. Co – morbidities
12. Chest symptoms :

	Yes/No	Duration
1. Cough	-	-
2. Expectoration	-	-
3. wheeze	-	-
4. Dyspnea	-	-
5. Chest tightness	-	-

GINA ASSESSMENT OF ASTHMA CONTROL

1. Any night waking due to asthma? Yes□ No□
2. Reliever needed more than twice/week? Yes□ No□
3. Any activity limitation due to asthma? Yes□ No□
4. Daytime asthma symptoms more than a week ?
   yes□No□

SPIROMETRY

HEIGHT WEIGHT

	PRE	BEST	%PRE	POST BD	PRE	%CHG
FVC						
FEV1						
FEV1/FVC						
PEF						
FEF25/75						

Impersion :

INVESTIGATION

SPUTUM EOSINOPHIL = %

ABSOLUTE BLOOD EOSINOPHIL = %

ஒப்புதல் படிவம்

என் நோயின் தன்மையை கண்டறிய சளி மற்றும் இரத்த பரிசோதனை அவசியம் என்பதை மருத்துவர் மூலம் தெரிந்து கொண்டேன். எனவே எனக்கு சளி மற்றும் இரத்தம் எடுத்து பரிசோதனை செய்ய முழு மனதுடன் சம்மதிக்கிறேன்.

நாள் :

இடம் :

இப்படிக்கு,

(நோயாளி / உறவினரின் கையொப்பம்)

S.No	NAME	AGE		SEX		RESIDENCE	OCCUPATION							ENVIRONMENT	
								BEEDIWORKER	TRUCTION WO	COTTON MILL	CKERS/FIREWO	OTHER			
1	perumal	31	2	m	1	thoothukudi	loadman	N	N	N	N	N		N	1
2	amavedivu	34	2	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
3	balammal	28	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
4	maharani	25	2	f	2	TIRUNELVELI	student	N	N	N	N	N		N	1
5	ibramin	42	3	m	1	TIRUNELVELI	gas worker	N	N	N	N	Y	5	Y	2
6	cristopher	42	3	m	1	TIRUNELVELI	chef	N	N	N	N	Y	5	Y	2
7	lakshmi	34	2	f	2	kovilpatti	beedi worker	Y	N	N	N	N	1	Y	2
8	selvi	38	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
9	surendharan	45	3	m	1	TIRUNELVELI	farmer	N	N	N	N	N		N	1
10	rani	40	2	f	2	kovilpatti	beedi worker	Y	N	N	N	N	1	Y	2
11	ganapathi	47	3	m	1	TIRUNELVELI	decoration worker	N	N	N	N	Y	5	Y	2
12	paramasivan	52	4	m	1	TIRUNELVELI	auto driver	N	N	N	N	N		N	1
13	rajaparvatham	39	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
14	patchiammal	49	3	f	2	TIRUNELVELI	farmer	N	N	N	N	N		N	1
15	kanagaraj	40	2	m	1	kovilpatti	mechanic	N	N	N	N	Y	5	Y	2
16	sornajayathi	40	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
17	mariya	43	3	f	2	NAGERKOVIL	farmer	N	N	N	N	N		N	1
18	thangaraj	54	4	m	1	kovipatti	fireworker	N	N	N	Y	N	4	Y	2
19	selvarani	40	2	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
20	mariammal	54	4	f	2	TIRUNELVELI	cotton mill worker	N	N	Y	N	N	3	Y	2
21	maragatham	47	3	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
22	simpson	35	2	m	1	TIRUNELVELI	shop worker	N	N	N	N	N		N	1
23	ravitheja	25	2	m	1	TIRUNELVELI	shop keeper	N	N	N	N	N		N	1
24	alagammal	32	2	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
25	siva	28	2	m	1	TIRUNELVELI	pipe manufacture	N	N	N	N	Y	5	Y	2
26	vidhya	28	2	f	2	TIRUNELVELI	sells worker	N	N	N	N	N		N	1
27	soraja	46	3	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
28	suruli	44	3	m	1	THOOTHUKUDI	fruit sellar	N	N	N	N	N		N	1
29	mukkammal	45	3	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
30	karuppasamy	29	2	m	1	TIRUNELVELI	field worker	N	N	N	N	N		N	1
31	essakipandi	38	2	f	2	TIRUNELVELI	construction worker	N	Y	N	N	N	2	Y	2
32	jasmin	23	1	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
33	MURUGAN	41	3	m	1	TIRUNELVELI	sugarcane juice maker	N	N	N	N	Y	5	Y	2
34	marisamy	54	4	m	1	THOOTHUKUDI	Construction worker	N	Y	N	N	N	2	Y	2
35	pathrakali	20	2	f	2	THOOTHUKUDI	student	N	N	N	N	N		N	1
36	mupidathi	58	4	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
37	santhosh	19	1	m	1	TIRUNELVELI	student	N	N	N	N	N		N	1
38	mookammal	55	4	f	2	TIRUNELVELI	farmer	N	N	N	N	N		N	1
39	shanmugavel	47	3	m	1	TOOTHUKUDI	bank manager	N	N	N	N	N		N	1

40	sudalayandi	52	4	m	1	TIRUNELVELI	auto driver	N	N	N	N	N		N	1
41	Geetha	45	3	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
42	Peer mohamed	40	2	m	1	TIRUNELVELI	cotton mill worker	N	N	Y	N	N	3	Y	2
43	kumaravel	29	2	m	1	TIRUNELVELI	electrician	N	N	N	N	N		N	1
44	shanthi	52	4	f	2	TIRUNELVELI	cotton mill worker	N	N	Y	N	N	3	Y	2
45	Kani	45	3	f	2	SIVAKASI	Crackers workers	N	N	N	Y	N	4	Y	2
46	chellakani	50	3	f	2	NAGERKOVIL	beedi worker	Y	N	N	N	N	1	Y	2
47	jothiram	45	3	f	2	THOOTHUKUDI	farmer	N	N	N	N	Y	5	Y	2
48	THULASI	18	1	f	2	TIRUNELVELI	student	N	N	N	N	N		N	1
49	Manikkam	34	2	m	1	NAGERKOVIL	daily wages	N	N	N	N	N		N	1
50	sundaram	56	4	m	1	THOOTHUKUDI	daily wages	N	N	N	N	N		N	1
51	Pushpa	33	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
52	marisamy	28	2	m	1	kovilpatti	mechanic	N	N	N	N	Y	5	Y	2
53	Mohamed Basha	45	3	m	1	TIRUNELVELI	construction worker	N	Y	N	N	N	2	Y	2
54	murugan	38	2	m	1	TIRUNELVELI	bag maker	N	N	N	N	N		N	1
55	JANSI	22	2	F	2	THOOTHUKUDI	student	N	N	N	N	N		N	1
56	ramar	39	2	m	1	TIRUNELVELI	construction worker	N	Y	N	N	N	2	Y	2
57	mannu goundar	49	3	m	1	kovilpatti	chef	N	N	N	N	Y	5	Y	2
58	sundhari	19	1	f	2	THOOTHUKUDI	cotton mill worker	N	N	Y	N	N	3	Y	2
59	kuppammal	56	4	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
60	anandhpillai	45	3	m	1	TIRUNELVELI	farmer	N	N	N	N	N		N	1
61	roobavathy	28	2	f	2	kovilpatti	HOUSEWIFE	N	N	N	N	N		N	1
62	kathappan	56	4	m	1	TIRUNELVELI	vegtable sellar	N	N	N	N	N		N	1

63	alagumurugan	36	2	m	1	TIRUNELVELI	farmer	N	N	N	N	N		N	1
64	ramsanthosh	33	2	m	1	TIRUNELVELI	auto driver	N	N	N	N	N		N	1
65	muppidathi	38	2	m	1	TIRUNELVELI	daily wages	N	N	N	N	N		N	1
66	kuppan	45	3	m	1	TIRUNELVELI	load man	N	N	N	N	N		N	1
67	parameshwari	28	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
68	subbammal	22	2	f	2	TIRUNELVELI	student	N	N	N	N	N		N	1
69	Tony singh	26	2	m	1	kovilpatti	chef	N	N	N	N	Y	5	Y	2
70	malayandi	41	3	m	1	TIRUNELVELI	daily wages	N	N	N	N	N		N	1
71	mariyammal	54	4	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
72	pushpam	52	4	f	2	NAGERKOVIL	HOUSEWIFE	N	N	N	N	N		N	1
73	ponnammal	35	2	f	2	THOOTHUKUDI	HOUSEWIFE	N	N	N	N	N		N	1
74	nisha	46	3	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2
75	muthukani	38	2	f	2	kovilpatti	beedi worker	Y	N	N	N	N	1	Y	2
76	saravanan	34	2	m	1	TIRUNELVELI	hotel server	N	N	N	N	N		N	1
77	kannan	35	2	m	1	kovilpatti	shop owner	N	N	N	N	N		N	1
78	poonkodi	32	2	f	2	TIRUNELVELI	HOUSEWIFE	N	N	N	N	N		N	1
79	sambu	28	2	m	1	TIRUNELVELI	auto driver	N	N	N	N	N		N	1
80	Thadikkaran	48	3	m	1	kovilpatti	plumber	N	N	N	N	Y	5	Y	2
81	sruthi	33	2	f	2	TIRUNELVELI	daily wages	N	N	N	N	N		N	1
82	maruthamalai	29	2	m	1	kovilpatti	auto driver	N	N	N	N	N		N	1
83	rhagavan	40	2	m	1	TIRUNELVELI	farmer	N	N	N	N	N		N	1
84	siddarth	38	2	m	1	TIRUNELVELI	hotel server	N	N	N	N	N		N	1
85	ganesan	43	3	m	1	TIRUNELVELI	Bsnl worker	N	N	N	N	N		N	1
86	murali	36	2	m	1	TIRUNELVELI	daily wages	N	N	N	N	N		N	1
87	shalini	35	2	f	2	NAGERKOVIL	HOUSEWIFE	N	N	N	N	N		N	1
88	malaiammal	42	3	f	2	TIRUNELVELI	vegtable sellar	N	N	N	N	N		N	1
89	manoj	22	2	m	1	kovilpatti	student	N	N	N	N	N		N	1
90	Esakkipandi	38	2	m	1	TIRUNELVELI	construction worker	N	Y	N	N	N	2	Y	2
91	ashok	30	2	m	1	kovilpatti	blumber	N	N	N	N	N		N	1
92	kumarimuthu	26	2	m	1	TIRUNELVELI	construction worker	N	Y	N	N	N	2	Y	2
93	pazhani	34	2	m	1	TIRUNELVELI	electrician	N	N	N	N	N		N	1
94	vaishali	18	1	f	2	kovilpatti	student	N	N	N	N	N		N	1
95	karukkuvelraja	25	2	m	1	TIRUNELVELI	sugarcane juice maker	N	N	N	N	Y	5	Y	2
96	THAMANNA	24	2	f	2	NAGERKOVIL	shop worker	N	N	N	N	N		N	1
97	lakshmi	34	2	f	2	THOOTHUKUDI	beedi worker	Y	N	N	N	N	1	Y	2
98	raja	22	2	m	1	kovilpatti	student	N	N	N	N	N		N	1
99	asainayagam	33	2	m	1	TIRUNELVELI	electrician	N	N	N	N	N		N	1
100	arichamy	38	2	m	1	THOOTHUKUDI	daily wages	N	N	N	N	N		N	1
101	kannammal	58	4	f	2	TIRUNELVELI	beedi worker	Y	N	N	N	N	1	Y	2

SMOKER		FAMILY H/O		ALLERGIC H/O						URT SYMPTOMS				
Yes	NO	YES	NO	Food	DUST	POLLEN	DRUGS	SEASONAL		Sneezing	AL CONGES	HEADACHE	RUNNING NOSE	SORE THROAT
1	0	1	0	1	2	2	1	2	2	2	2	1	2	2
0	1	0	1	1	2	1	1	1	2	2	2	2	2	1
0	1	1	0	1	2	2	1	2	2	2	2	1	2	1
0	1	1	0	1	2	2	1	2	2	2	2	1	2	1
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1	0	1	0	1	2	1	1	2	2	2	2	1	2	1
0	1	1	0	1	1	1	1	2	4	1	1	1	1	1
0	1	0	1	1	2	1	1	1	2	2	2	2	2	1
1	0	0	1	1	1	1	1	2	4	1	1	1	1	1
0	1	0	1	1	2	2	1	2	2	2	2	1	2	1
0	1	0	1	1	2	2	1	2	2	2	2	1	2	1
0	1	1	0	1	2	1	1	2	2	2	2	2	2	1
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0	1	1	0	1	2	2	1	2	2	1	2	1	2	1
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0	1	1	0	1	2	2	1	2	2	1	2	1	1	1
1	0	1	0	1	1	1	1	2	4	2	2	1	2	1

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0	1	0	1	1	1	1	1	2	4	1	1	1	2	2
0	1	0	1	1	2	1	1	1	2	1	1	1	1	1
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0	1	1	0	1	2	2	1	2	2	2	2	1	2	1
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0	1	0	1	1	2	1	1	2	2	2	1	1	2	1
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0	1	0	1	1	2	1	1	2	2	2	1	1	2	1
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0	1	1	0	1	2	2	1	2	2	2	2	1	2	1
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0	1	1	0	1	1	1	1	2	4	1	1	1	1	1
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0	1	1	0	1	2	1	1	2	2	2	1	1	2	1
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0	1	1	0	1	1	1	1	2	4	2	2	1	1	2
0	1	0	1	1	2	1	1	2	2	2	2	1	2	2

HISTORY											
				CO-MORBID	COUGH		EXPECTORATION		WHEEZE		D
Obesity	GERD	OSA	RHINOSINUSITIS	PRESSION/ANXIE	YES / NO	If yes, Duration	YES / NO	If yes, Duration	YES / NO	If yes, Duration	YES / NO
1	1	1	2	1	YES	20	YES	20	YES	20	YES
1	1	1	2	1	YES	15	YES	15	YES	15	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	3	YES	3	YES	3	YES
1	2	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	8	YES	8	YES	8	YES
1	1	1	1	1	YES	8	YES	8	YES	8	YES
1	2	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	2	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	20	YES	20	YES	20	YES
1	1	1	2	2	YES	10	YES	10	YES	10	YES
1	1	2	1	1	YES	11	YES	11	YES	11	YES
1	2	1	2	1	YES	5	YES	5	YES	5	YES
1	2	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	30	YES	30	YES	30	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	20	YES	20	YES	20	YES
1	1	1	2	1	YES	14	YES	14	YES	14	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	8	YES	8	YES	8	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	15	YES	15	YES	15	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	8	YES	8	YES	8	YES
1	2	1	1	1	YES	10	YES	10	NO	0	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	4	YES	4	NO	0	YES
1	2	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	2	2	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	8	YES	8	NO	0	YES

1	1	1	2	1	YES	1	YES	1	YES	1	YES
1	2	1	1	1	YES	2	YES	2	YES	2	YES
2	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	2	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	6	YES	6	YES	6	YES
1	1	1	2	1	YES	2	YES	2	YES	2	YES
1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	1	2	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	2	YES	2	YES	2	YES
1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	2	1	1	1	YES	1	YES	1	YES	1	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	2	1	YES	1	YES	1	YES	1	YES
1	1	1	2	1	YES	1	YES	1	YES	1	YES
1	2	1	1	1	YES	4	YES	4	YES	4	YES
1	2	1	2	1	YES	8	YES	8	YES	8	YES
1	1	1	1	1	YES	1	YES	1	YES	1	YES
1	1	1	1	2	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	2	1	1	1	YES	3	YES	3	YES	3	YES

1	1	1	1	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	2	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	6	YES	6	YES	6	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	6	YES	6	YES	6	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	2	1	YES	5	YES	5	YES	5	YES
1	1	1	2	1	YES	8	YES	8	YES	8	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	1	2	YES	1	YES	1	YES	1	YES
1	1	1	1	1	YES	6	YES	6	YES	6	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	2	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	1	YES	1	YES	1	YES
1	1	1	1	2	YES	8	YES	8	YES	8	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	2	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	1	YES	1	YES	1	YES
1	1	1	2	1	YES	5	YES	5	YES	5	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	2	1	1	1	YES	1	YES	1	YES	1	YES
1	1	1	2	1	YES	10	YES	10	YES	10	YES
1	1	1	1	1	YES	3	YES	3	YES	3	YES
1	1	1	1	1	YES	4	YES	4	YES	4	YES
1	2	1	1	1	YES	10	YES	10	YES	10	YES

)YSPNEA	CHEST TIGHTNESS		NO .EXACERBATION	TREATMENT H/O			GINA ASSESSMENT				
If yes, Duration	YES / NO	f yes, Duratio		OW DOSE ST	DOSE STEROIDS ICS/	IGH DOSE ST	Night C/o	Reliever >2/w	Limitation	y time c/o >2	score
20	YES	20	5	0	0	1	0	1	1	1	3
15	YES	15	5	0	0	1	1	1	1	1	4
10	YES	10	4	0	1	0	1	1	1	1	4
3	YES	3	3	0	0	1	1	1	1	1	4
5	YES	5	4	0	0	1	1	1	1	1	4
3	YES	3	1	1	0	0	0	0	0	0	0
8	YES	8	4	0	0	1	1	1	1	0	3
8	YES	8	3	0	1	0	1	1	1	0	3
3	YES	3	2	1	0		1	0	0	0	1
10	YES	10	4	0	0	1	1	1	1	0	3
3	YES	3	3	0	1	0	1	1	1	0	3
5	YES	5	6	0	0	1	1	1	1	1	4
10	YES	10	4	0	1	0	0	0	0	0	3
5	YES	5	3	0	1	0	1	1	1	1	4
20	YES	20	5	0	1	0	1	1	1	0	3
10	YES	10	5	0	0	1	0	1	1	0	3
11	YES	11	3	0	1	0	1	1	1	1	4
5	YES	5	4	0	1	0	0	1	1	1	3
4	YES	4	4	0	0	1	1	1	1	1	4
3	YES	3	5	0	1	0	0	1	1	0	3
30	YES	30	7	0	1	0	1	0	1	1	3
3	YES	3	5	0	1	0	1	0	1	0	3
10	YES	10	1	1	0	0	1	0	0	1	2
20	YES	20	4	0	1	0	0	0	0	1	3
14	YES	14	3	0	1	0	1	1	1	1	4
10	YES	10	2	0	1		0	0	0	0	0
8	YES	8	3	0	1	0	1	1	1	1	4
3	YES	3	2	1	0	0	0	0	0	0	0
15	YES	15	4	0	1	0	0	1	1	0	3
10	YES	10	3	0	1	0	0	0	1	1	3
3	YES	3	3	0	1	0	1	1	1	1	4
8	YES	8	3	0	1	0	1	1	1	1	4
10	NO	0	3	0	1	0	1	1	1	0	3
10	YES	10	4	0	1	0	1	1	1	1	3
4	YES	4	3	0	1	0	1	1	0	1	3
5	YES	5	3	0	1	0	0	1	1	1	3
10	YES	10	3	0	1	0	1	0	1	0	3
3	NO	0	4	0	1	0	1	1	1	1	4
8	NO	0	3	0	1	0	1	1	1	1	4

1	YES	1	1	1	0	0	1	0	0	0	1
2	YES	2	1	1	0	0	1	0	0	0	1
10	YES	10	6	0	1	0	1	1	1	1	4
5	NO	0	3	0	1	0	1	0	0	0	3
5	YES	5	4	0	1	0	1	1	1	1	4
10	YES	10	3	0	0	1	1	1	1	1	4
4	YES	4	3	0	1	0	0	1	1	0	3
6	YES	6	6	0	1	0	1	1	1	0	3
2	YES	2	2	1	0	0	1	0	0	0	1
5	NO	0	1	1	0	0	1	0	0	0	1
10	YES	10	2	1	0	0	1	0	0	1	2
2	YES	2	1	1	0	0	1	0	0	0	1
5	NO	0	1	0	1		1	0	0	0	1
1	YES	1	2	1	0	0	1	0	0	0	1
4	YES	4	3	0	0	1	1	1	1	1	4
1	YES	1	1	1	0	0	1	0	0	0	1
1	YES	1	2	0	1		1	0	0	0	1
4	YES	4	2	1	0	0	0	0	0	0	0
8	YES	8	4	0	1	0	1	1	1	1	4
1	YES	1	2	1	0	0	1	0	0	0	1
3	YES	3	1	0	1		1	0	0	0	1
3	YES	3	1	1	0	0	1	0	1	0	2
3	YES	3	1	1	0	0	1	0	0	0	1

5	NO	0	3	0	1	0	1	1	1	1	3
3	YES	3	2	1	0	0	1	0	0	0	1
10	YES	10	2	0	1		0	0	0	0	0
4	YES	4	1	0	1		1	0	0	1	2
10	YES	10	3	0	1	0	1	0	0	0	3
4	YES	4	4	0	1	0	1	0	0	1	3
6	YES	6	3	0	1	0	1	0	0	1	3
10	YES	10	5	0	1	0	1	0	0	1	3
5	YES	5	1	0	1		1	0	0	1	2
6	YES	6	3	0	1	0	1	1	1	1	4
4	YES	4	5	0	1	0	1	0	0	0	3
5	YES	5	3	0	1	0	0	1	1	0	3
8	YES	8	3	0	1	0	1	1	1	1	4
10	YES	10	1	0	1	0	1	0	0	0	1
10	YES	10	1	0	1		1	0	0	1	2
3	YES	3	1	0	1		1	0	0	0	1
10	YES	10	2	0	1		0	0	0	0	0
1	NO	0	2	1	0	0	0	0	0	0	0
6	YES	6	4	0	1	0	1	0	0	1	3
4	YES	4	2	0	1		1	0	0	0	1
5	NO	0	2	0	1		1	0	0	0	1
1	YES	1	2	0	1		0	0	0	0	0
8	YES	8	5	0	1	0	1	1	1	1	4
3	YES	3	2	1	0	0	1	0	0	0	1
3	YES	3	2	0	1		1	0	0	0	1
10	YES	10	4	0	1	0	1	1	1	1	4
3	YES	3	1	0	1		1	0	0	1	2
3	YES	3	1	0	1		1	1	1	0	3
4	YES	4	1	0	1		1	0	0	1	2
10	YES	10	1	0	1		1	0	0	0	1
1	YES	1	2	0	1		0	0	0	0	0
5	NO	0	1	0	1		1	0	0	0	1
4	YES	4	1	0	1		1	0	0	0	1
4	NO	0	1	1	0	0	1	0	0	1	2
1	YES	1	2	0	1		1	1	1	0	2
10	NO	0	5	0	1	0	1	0	0	1	3
3	YES	3	3	0	1	0	1	0	0	0	3
4	YES	4	3	0	1	0	0	0	0	0	3
10	YES	10	4	0	0	1	1	1	1	1	4

EXAMINATION											
		Ht (m)	Wt(kg)	BMI	RS EXAMINATION			spo2 %	SPIROMETRY		
				normal /no added s	CRAKLES	WHEEZE			FVC	FEV1	
2	2	1.7	60	20.76124567	1	1	2	97	90	33	3
2	2	1.6	50	19.53125	1	1	2	92	78	21	3
2	2	1.44	44	21.2191358	1	1	2	94	77	42	3
2	2	1.57	45	18.25631871	1	1	2	94	67	28	3
2	2	1.67	70	25.0995016	1	1	2	92	80	24	3
1	1	1.64	63	23.42355741	1	1	2	97	93	86	1
2	2	1.6	62	24.21875	1	1	2	94	87	26	3
2	2	1.6	70	27.34375	1	1	2	94	90	47	3
1	1	1.5	50	22.22222222	1	1	2	96	90	67	2
2	2	1.5	72	32	1	1	2	92	93	29	3
2	2	1.57	64	25.96454217	1	1	2	97	90	40	3
2	2	1.75	61	19.91836735	1	1	2	94	65	31	3
2	1	1.6	70	27.34375	1	1	2	96	90	58	3
2	2	1.53	55	23.49523687	1	1	2	94	90	39	3
2	2	1.6	55	21.484375	1	1	2	98	98	41	3
2	1	1.6	68	26.5625	1	1	2	96	90	35	3
2	2	1.5	68	30.22222222	1	1	2	93	90	36	3
2	2	1.7	74	25.60553633	1	1	2	94	83	38	3
2	2	1.7	80	27.6816609	1	1	2	94	90	28	3
2	1	1.8	86	26.54320988	1	1	2	97	45	50	3
2	2	1.5	60	26.66666667	1	1	2	96	90	41	3
2	1	1.5	65	28.88888889	1	1	2	95	90	56	3
1	1	1.52	54	23.37257618	1	1	2	96	90	96	1
2	1	1.4	59	30.10204082	1	2	2	94	68	54	3
2	2	1.66	54	19.59645812	1	1	2	94	55	45	3
1	1	1.53	55	23.49523687	1	1	2	97	78	70	2
2	2	1.65	66	24.24242424	1	1	2	94	62	47	3
1	1	1.62	59	22.48132907	1	1	2	96	90	94	1
2	1	1.6	50	19.53125	1	1	2	94	90	49	3
2	1	1.7	69	23.87543253	1	1	2	94	100	50	3
2	2	1.5	65	28.88888889	1	1	2	96	90	48	3
2	2	1.56	34	13.97107166	1	1	2	96	66	42	3
2	2	1.6	64	25	2	1	1	97	96	40	3
2	2	1.7	60	20.76124567	1	1	2	96	50	40	3
2	2	1.56	34	13.97107166	1	1	2	94	70	44	3
2	2	1.6	70	27.34375	1	1	2	92	90	37	3
2	1	1.7	80	27.6816609	1	1	2	97	90	59	3
2	2	1.64	60	22.30814991	1	1	2	94	90	37	3
2	2	1.7	64	22.14532872	1	1	2	94	128	48	3

1	1	1.58	45	18.02595738	1	1	2	97	94	90	1
1	1	1.56	60	24.65483235	1	1	2	97	90	80	1
2	2	1.55	48	19.97918835	1	1	2	96	46	41	3
2	1	1.67	70	25.0995016	1	1	2	95	90	55	3
2	2	1.61	36	13.88835307	1	1	2	97	72	43	3
2	2	1.47	49	22.67573696	1	1	2	96	100	34	3
2	1	1.6	64	25	1	1	2	94	90	52	3
2	2	1.68	60	21.2585034	1	1	2	94	77	46	3
1	1	1.6	46	17.96875	1	1	2	97	90	88	1
1	1	1.7	74	25.60553633	1	1	2	97	90	81	1
1	1	1.76	80	25.82644628	1	1	2	95	90	82	1
1	1	1.55	56	23.30905307	1	1	2	95	90	83	1
1	1	1.5	68	30.22222222	1	1	2	96	90	67	2
1	1	1.58	48	19.22768787	1	1	2	96	90	85	1
2	2	1.6	50	19.53125	1	1	2	97	90	32	3
1	1	1.64	58	21.56454491	1	1	2	97	90	87	1
1	1	1.5	60	26.66666667	1	1	2	94	77	72	2
1	1	1.54	50	21.08281329	1	1	2	97	90	91	1
2	2	1.49	44	19.81892708	1	1	2	96	72	42	3
1	1	1.55	58	24.14151925	1	1	2	97	96	93	1
1	1	1.62	52	19.81405274	1	1	2	97	90	79	2
1	1	1.64	56	20.82093992	1	1	2	97	94	84	1
1	1	1.72	62	20.9572742	1	1	2	97	94	95	1

2	2	1.58	80	32.04614645	1	1	2	94	100	55	3
1	1	1.57	59	23.93606231	1	1	2	97	90	97	1
1	1	1.65	66	24.24242424	1	1	2	95	93	78	2
1	1	1.6	70	27.34375	1	1	2	97	90	68	2
2	1	1.57	45	18.25631871	1	1	2	95	90	51	3
2	1	1.6	50	19.53125	1	1	2	96	90	52	3
2	1	1.7	60	20.76124567	1	1	2	97	90	53	3
2	1	1.44	44	21.2191358	1	1	2	97	90	54	3
1	1	1.7	60	20.76124567	1	1	2	96	98	73	2
2	2	1.52	40	17.31301939	1	1	2	96	45	46	3
2	1	1.6	62	24.21875	1	1	2	97	90	57	3
2	1	1.5	66	29.33333333	2	1	1	94	110	48	3
2	2	1.44	44	21.2191358	1	1	2	94	99	43	3
1	1	1.5	72	32	1	1	2	97	90	60	2
1	1	1.57	64	25.96454217	1	1	2	97	90	61	2
1	1	1.75	61	19.91836735	1	1	2	96	90	62	2
1	1	1.6	50	19.53125	1	1	2	97	90	63	2
1	1	1.74	82	27.08415907	1	1	2	96	90	98	1
2	1	1.62	66	25.1486054	1	1	2	97	90	50	3
1	1	1.7	60	20.76124567	1	1	2	97	90	64	2
1	1	1.5	69	30.66666667	1	1	2	95	90	65	2
1	1	1.6	68	26.5625	1	1	2	97	90	66	2
2	2	1.68	54	19.13265306	1	1	2	94	94	49	3
1	1	1.62	52	19.81405274	1	1	2	95	90	92	1
1	1	1.7	74	25.60553633	1	1	2	96	67	69	2
2	2	1.5	40	17.77777778	1	1	2	94	90	43	3
1	1	1.8	86	26.54320988	1	1	2	94	50	71	2
2	2	1.68	55	19.48696145	1	1	2	97	80	65	2
1	1	1.6	64	25	1	1	2	94	80	73	2
1	1	1.44	44	21.2191358	1	1	2	96	90	74	2
1	1	1.4	59	30.10204082	1	1	2	97	87	75	2
1	1	1.66	54	19.59645812	1	1	2	94	90	76	2
1	1	1.68	60	21.2585034	1	1	2	94	90	77	2
1	1	1.58	54	21.63114885	1	1	2	96	90	89	1
1	2	1.48	42	19.17457999	1	1	2	95	74	66	2
2	1	1.55	58	24.14151925	1	1	2	94	65	50	3
2	1	1.62	59	22.48132907	1	1	2	94	90	54	3
2	1	1.6	50	19.53125	1	1	2	95	90	56	3
2	2	1.5	69	30.66666667	1	1	2	98	80	34	3

INVESTIGATION									
		CHEST XRAY				SPUTUM EOSINOPHIL %	ABSOLUTE BLOOD EOSINOPHIL		
FEV1/FVC(Pre)	significant reversiblity(>12%)	NORMAL	RINFLATED	ONCHIECTA	FIBROSIS			Severity	
70	present	2	1	1	1	3	350	severe	3
58	present	1	2	1	1	4	300	severe	3
59	present	1	2	1	1	2	420	severe	3
60	present	1	2	1	1	3	500	severe	3
62	present	2	1	1	1	2	350	severe	3
60	present	2	1	1	1	0	300	mild	1
59	present	1	2	1	1	1	150	severe	3
60	present	1	2	1	1	0	300	severe	3
68	present	2	1	1	1	0	150	moderate	2
70	present	2	1	1	1	1	780	severe	3
60	present	2	1	1	1	0	100	severe	3
50	present	1	1	1	2	3	970	severe	3
68	present	2	1	1	1	3	400	severe	3
68	present	1	2	1	1	2	400	severe	3
60	present	1	2	1	1	2	420	severe	3
60	present	2	1	1	1	2	250	severe	3
60	present	1	2	1	1	2	300	severe	3
92	present	1	2	1	1	3	750	severe	3
60	present	2	1	1	1	2	300	severe	3
66	present	2	1	1	1	4	300	severe	3
60	present	1	2	1	1	1	300	severe	3
70	present	1	2	1	1	2	400	severe	3
62	present	2	1	1	1	0	210	mild	1
68	present	1	1	2	1	3	300	severe	3
66	present	2	1	1	1	0	250	severe	3
56	present	2	1	1	1	1	500	moderate	2
64	present	2	1	1	1	3	300	severe	3
66	present	2	1	1	1	1	140	mild	1
60	present	1	2	1	1	2	350	severe	3
68	present	1	2	1	1	1	300	severe	3
89	present	2	1	1	1	2	300	severe	3
68	present	2	1	1	1	2	200	severe	3
70	present	1	2	1	1	3	250	severe	3
69	present	2	1	1	1	4	800	severe	3
64	present	1	2	1	1	2	150	severe	3
80	present	1	2	1	1	3	300	severe	3
66	present	1	2	1	1	0	150	severe	3
54	present	1	2	1	1	1	200	severe	3
64.6	present	1	2	1	1	2	350	severe	3

62	present	2	1	1	1	1	90	mild	1
64	present	2	1	1	1	1	200	mild	1
52	present	1	2	1	1	5	500	severe	3
60	present	1	2	1	1	1	210	severe	3
64	present	2	1	1	1	1	150	severe	3
60.5	present	1	2	1	1	2	350	severe	3
70	present	2	1	1	1	0	300	severe	3
58	present	1	2	1	1	1	250	severe	3
60	present	2	1	1	1	0	260	mild	1
62	present	2	1	1	1	0	240	mild	1
66	present	2	1	1	1	0	100	mild	1
63	present	2	1	1	1	1	200	mild	1
69	present	2	1	1	1	3	200	moderate	2
60	present	2	1	1	1	0	120	mild	1
70	present	2	1	1	1	3	300	severe	3
67	present	2	1	1	1	1	270	mild	1
64.6	present	2	1	1	1	1	500	moderate	2
70	present	2	1	1	1	0	170	mild	1
68	present	1	2	1	1	2	400	severe	3
69	present	2	1	1	1	0	300	mild	1
64	present	2	1	1	1	1	160	moderate	2
65	present	2	1	1	1	0	150	mild	1
67	present	2	1	1	1	0	180	mild	1

68	present	2	1	1	1	1	200	severe	3
64	present	2	1	1	1	0	170	mild	1
68	present	1	2	1	1	2	200	moderate	2
64	present	1	2	1	1	3	300	moderate	2
80	present	1	2	1	1	2	200	severe	3
92	present	2	1	1	1	1	300	severe	3
68	present	1	2	1	1	1	250	severe	3
66	present	2	1	1	1	2	300	severe	3
65	present	2	1	1	1	2	180	moderate	2
56	present	2	1	1	1	1	750	severe	3
70	present	2	1	1	1	3	220	severe	3
58	present	1	2	1	1	2	223	severe	3
70	present	2	1	1	1	2	350	severe	3
58	present	1	2	1	1	1	200	moderate	2
64	present	1	2	1	1	2	500	moderate	2
58	present	2	1	1	1	0	180	moderate	2
60	present	1	2	1	1	1	500	moderate	2
66	present	2	1	1	1	0	230	mild	1
60	present	2	1	1	1	1	110	severe	3
68	present	2	1	1	1	1	200	moderate	2
60	present	1	2	1	1	2	330	moderate	2
68	present	2	1	1	1	1	280	moderate	2
62.3	present	1	2	1	1	2	500	severe	3
62	present	2	1	1	1	1	200	mild	1
68	present	1	2	1	1	1	140	moderate	2
69	present	2	1	1	1	1	320	severe	3
54	present	1	2	1	1	2	190	moderate	2
58	present	1	2	1	1	3	350	moderate	2
62.3	present	1	2	1	1	0	380	moderate	2
70	present	2	1	1	1	1	330	moderate	2
52	present	1	2	1	1	2	240	moderate	2
58	present	2	1	1	1	0	780	moderate	2
55	present	1	2	1	1	1	480	moderate	2
68	present	2	1	1	1	0	180	mild	1
55	present	1	2	1	1	3	450	moderate	2
62	present	1	2	1	1	1	420	severe	3
66	present	2	1	1	1	3	210	severe	3
63	present	1	2	1	1	2	400	severe	3
68	present	1	2	1	1	1	200	severe	3